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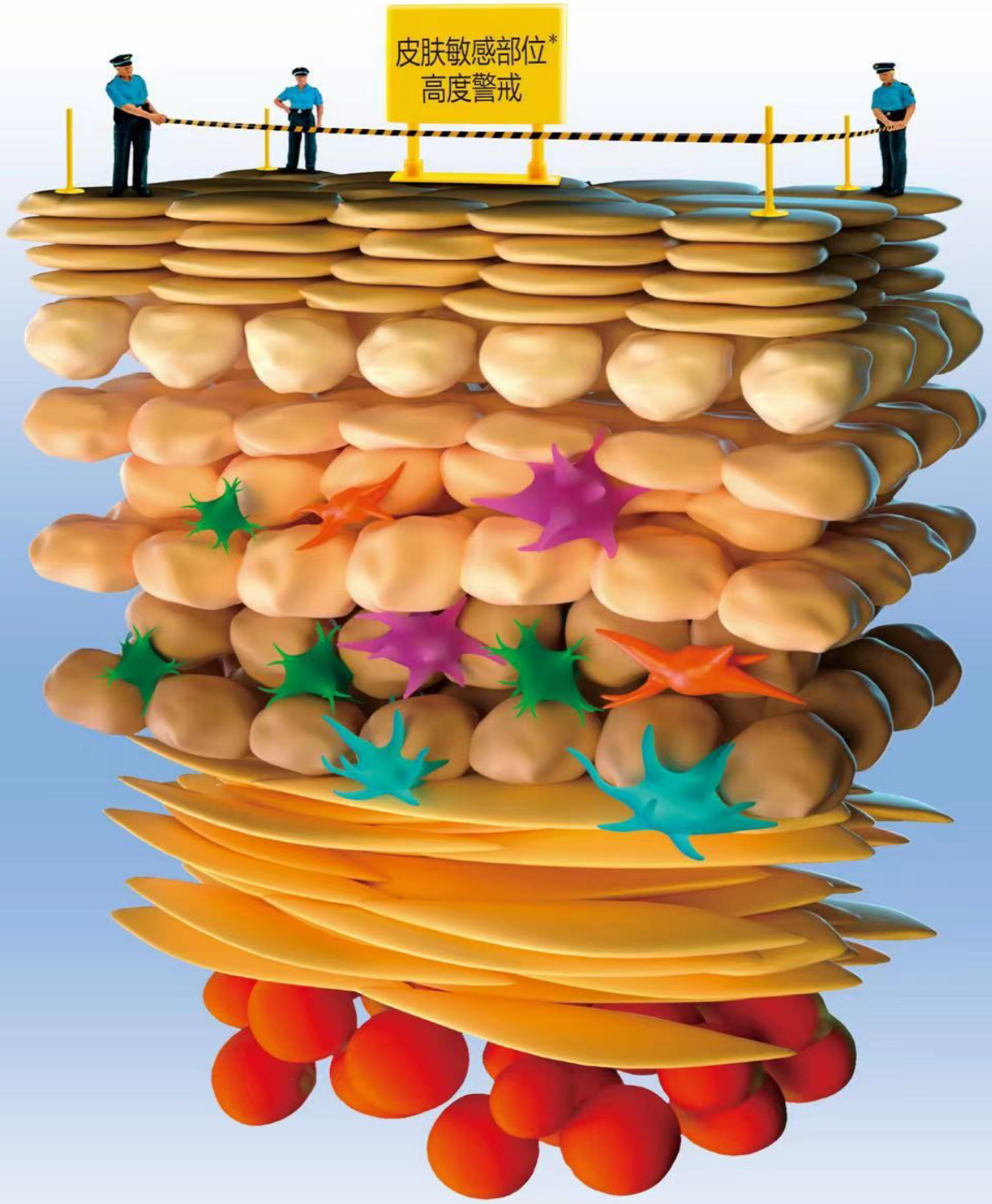

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Pulmonology

呼吸

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Clinical characteristics of community-acquired pneumonia in children

Jie Li*、Xinrong Sun
Xi 'an Children's Hospital

Abstract Content To analyze the case data of children with community-acquired pneumonia (CAP) and master its main clinical features, so as to provide reference for clinical diagnosis.

Methods The clinical data of symptoms, signs and imaging examination of 82 hospitalized children who met the diagnostic criteria of community-acquired pneumonia in Xi 'an Children's Hospital from October 4 to November 24, 2019 were collected and analyzed statistically

Results Among the 82 children, there were 43 males (51.8%) and 39 females (47.0%). According to age group, there were 6 infants, 23 infants, 30 preschool children, 23 school-age and adolescent children, with an average age of (4.64±2.99) years, especially preschool children. The average total hospitalization days of the children in this group were (12.27±8.08) days, during which they all had cough, 78 cases (95.1%) had different degrees of fever, and the average peak value of body temperature was (37.5±8.6)℃. Some patients had dysphoria, asthma, shortness of breath and other serious complications such as myocardial damage, pleural effusion, pericardial effusion and type I respiratory failure. Among them, 38 cases (46.3%) showed poor spirits, 17 cases (20.7%) showed cyanosis or three concave signs (+), 16 cases (19.5%) could hear wheezing sounds in auscultation of the lungs, and 28 cases (34.1%) could hear phlegm-dampness sounds in different degrees. Etiological examination showed that 49 cases (59.8%) were infected with mycoplasma pneumoniae, respiratory syncytial virus, influenza virus, adenovirus and other pathogens. The positive rate of mycoplasma pneumoniae in children over 3 years old was higher than that in children under 3 years old, with significant difference ($P < 0.01$). Inflammatory indexes such as white blood cell count, C-reactive protein, PCT and erythrocyte sedimentation rate increased in different degrees in laboratory examination. Chest imaging examination showed that 58 cases (70.7%) showed patchy shadows, fibrous cord changes or consolidation of lung, especially lobar pneumonia, mainly on the left side. There were 53 cases of common pneumonia and 29 cases of severe pneumonia in this group. On the basis of symptomatic treatment, all children with severe pneumonia were treated with intravenous immunoglobulin support or hormone anti-inflammatory, and all the children were improved or cured.

Conclusion Among the children with community acquired pneumonia in our hospital, preschool age is more common, and boys are more than girls. Common pathogens of CAP include mycoplasma pneumoniae, influenza virus, respiratory syncytial virus, adenovirus, etc. Mycoplasma pneumoniae infection is more common in preschool age and above. Different pathogens have different clinical symptoms, so strengthening individualized diagnosis and treatment thinking is of great clinical significance to the assessment and treatment of children's community-acquired pneumonia.

Key words Children; Community acquired pneumonia; clinical features
Reference

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Clinical characteristics of 32 cases of adenovirus pneumonia

Jie Li*、Xinrong Sun、Yali Fan
Xi 'an Children's Hospital

Abstract Content To summarize and analyze the clinical characteristics of children with adenoviral pneumonia, and provide basis for early and correct treatment of adenoviral pneumonia

Methods The clinical data of 32 children with adenoviral pneumonia diagnosed in Xi 'an Children's Hospital from October 1, 2019 to December 31, 2019 were analyzed retrospectively, and were divided into mild group and severe group according to clinical characteristics

Results The average age of 32 children with adenoviral pneumonia was (3.84±2.36) years old, and they all had fever during the course of disease, with an average peak value of (39.95±0.76)℃, the heat journey was mostly about 1-2 weeks, and the average hospital stay was (16.16±12.52) days. Besides cough, asthma and other symptoms, pleural effusion also appeared in severe cases. Compared with mild group, chest CT in severe group mainly involved bilateral lung fields, with significant statistical difference (P <0.01). Nine patients with pleural effusion were all children in severe group (P<0.05). A few patients were accompanied by focal atelectasis. In the severe group, the average hospitalization days of 4 children with adenovirus type 7 pneumonia were (39.75±19.03) days, and the average peak temperature was (40.65±1.03)℃, which mainly showed obvious dysphoria and listlessness, cyanosis in the mouth or face, audible lung, different degrees of lung wheezing and positive three concave signs, and one case complicated with toxic encephalopathy. Imaging examination showed that bilateral lung fields were involved with pleural effusion of different degrees, which indicated that the clinical symptoms and indexes were more severe than that of 1 case with type 3 disease. All patients were treated with antiviral therapy, and some patients were treated with methylprednisolone anti-inflammatory therapy and gamma globulin support. All patients were improved or cured and discharged from hospital

Conclusion The clinical manifestations of adenoviral pneumonia are severe and may be accompanied by serious complications. The combination of clinical features, imaging examination and virus typing can help to evaluate the severity of the disease.

Key words Children; Adenovirus pneumonia; clinical features
Reference

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Mutations in CCNO result in Primary ciliary dyskinesia complicated with diffuse bronchiolitis: a case report and literature review

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Background: Primary ciliary dyskinesia (PCD) is a rare genomic disorder with a phenotype heterogeneity that depends upon the genotype. Critical gene mutants like CCNO can trigger severe respiratory disease, but limited data have been available until now.
Methods: We received a patient with neonatal respiratory distress at birth and who had experienced a cough with accompanying wheeze for eight years. A high-resolution computed tomography scan of the patient’s chest showed special findings that evolved year by year. According to the clinical and imaging findings, screenings of PCD-related genes revealed a compound heterozygous mutation of CCNO. We analyzed the genotype- and phenotype-oriented literature of CCNO-related PCD and compared the reported findings to those of our case.
Results: A total of 43 patients with CCNO-related PCD from 30 families were reviewed and analyzed. Approximately 57.1% (24/42) of these patients were born in families where consanguineous marriage had occurred. Most patients experienced symptoms as neonates (85.3%). Recurrent respiratory tract infection (83.3%), neonatal respiratory distress (69.0%), and sinusitis/rhinorrhea (50.0%) were major manifestations, with chronic cough (35.7%), and recurrent otitis media (28.6%) being less common. Hearing loss, infertility, congenital heart defects, and hydrocephalus were even more rare, and heterotaxy was never seen. Bronchiectasis was the most common radiologic finding, while the patient in our study had presented with special findings of small diffuse nodules in both lungs, similar to diffuse pan-bronchiolitis (DPB). Thirteen different CCNO variants were identified, with most located in exon 1 (79.1%, 34/43), and c.258_262dupGGCCC mutation was the most common variant. Our participant had previously been diagnosed with c.263_267dupAGCCC and c.258_262dupGGCCC mutations from her mother and father, respectively.
Conclusion: CCNO variants are rare in PCD patients but lead to more severe phenotypes than other genes. Neonatal respiratory distress is common, and diffuse bronchiolitis could be the primary radiologic feature of CCNO-related PCD.

关键字 Primary ciliary dyskinesia; Cyclin O(CCNO); diffuse bronchiolitis; children

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Comparison of 11 respiratory pathogens among hospitalized children before and after the COVID-19 epidemic in Shenzhen, China

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Objectives: The effect of SARS-CoV-2 on existing respiratory pathogens in circulation remains uncertain. This study aimed to assess the impact of SARS-CoV-2 on the prevalence of respiratory pathogens among hospitalized children.
Methods: This study enrolled hospitalized children with acute respiratory infections in Shenzhen Children's Hospital from September to December 2019 (before the COVID-19 epidemic) and those from September to December 2020 (after the COVID-19 epidemic). Nasopharyngeal swabs were collected, and respiratory pathogens were detected using multiplex PCR. The absolute case number and detection rates of 11 pathogens were collected and analyzed.
Results: A total of 5696 children with respiratory tract infection received multiplex PCR examination for respiratory pathogens: 2298 from September to December 2019 and 3398 from September to December 2020. At least one pathogen was detected in 1850 (80.5%) patients in 2019, and in 2380 (70.0%) patients in 2020; the detection rate in 2020 was significantly lower than that in 2019. The detection rates reflected changes in these pathogens after the COVID-19 epidemic. The Influenza A (InfA) detection rate was 5.6% in 2019, but 0% in 2020. The detection rates of Mycoplasma pneumoniae, Human adenovirus, and Human rhinovirus also decreased from 20% (460), 8.9% (206), and 41.8% (961) in 2019 to 1.0% (37), 2.1% (77), and 25.6% (873) in 2020, respectively. In contrast, the detection rates of Human respiratory syncytial virus, Human parainfluenza virus, and Human metapneumovirus increased from 6.6% (153), 9.9% (229), and 0.5% (12) in 2019 to 25.6% (873), 15.5% (530), and 7.2% (247) in 2020, respectively ($p < 0.0001$).
Conclusions: The emergence of SARS-CoV-2 was associated with the substantial reduction in the circulation of respiratory pathogens including influenza virus, rhinovirus, adenovirus, and Mycoplasma pneumoniae, as well as with the increase in respiratory syncytial virus, parainfluenza, and human metapneumovirus in Shenzhen. The reasons for this phenomenon require further studies.

关键字 COVID-19； respiratory pathogens；children

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Myocardin regulates the structural changes and airway functional responses in asthma

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Aim: An increased number of airway myocytes (hyperplasia) and an enhanced contractile capacity (hypertrophy) contribute to the thickening of airway smooth muscle (ASM). The increased ASM mass in the asthmatic airways is likely to be only partially reversible with common anti-inflammation medications, so transcription factors contributing to ASM remodeling could be potential therapeutic targets for symptom allievation. Myocardin (myocd) is a key transcription factor for the phenotypic modulation of smooth muscle cells . Myocd coordiantes with its specific coactivators to promote the expression of contractile related genes in airway smoothe cells.
Method: Myocd was specifically knockout in lung mesenchyme by using the Tbx4-rtTA/Teto-Cre driver line to generate the Myocd coditional knockout mice (CKO)..A chronic asmatic model was then established by intraperitoneal (IP) injection of OVA + ALUM and intratracheal OVA challenging . Lung biopsies were obtained 24h after the lastchallenge. Lung specimens were stained with Haemotoxylin and Eosin, and PAS-Alcian blue to assess the difference in cell proliferation, contraction and hypertrophy of airway smooth muscle cells and the mucous secretion between CKO and wild type (WT) mice. Immunofluorescence staining of the α-smooth muscle actin(α-SMA) ,Ki67 and DAPI were used to evaluate the altered SMC structure in the CKO lungs. Lung function test was applied to determine the airway restriction in myocd knockouted mice..
Result:Myocd knockout was validated by DNA genotyping. After the sensitization of OVA + ALUM and the challenging of OVA, PAS-Alcian blue staining showed the airway of WT mice was significant contracted and the mucous secretion was decreased in CKO mice, the airway space is extend in CKO mice. HE staining showed the numbers of proliferative inflamation cells within the CKO was significantly decreased from WT. Immunofluorescence staining exhibited the ASM discontinuty and thinner. The hypertrophy ,hyperplasia and proliferation of ASM can be reduced in the CKO. Knockout myocd in ASM can also reduce the proliferation of airway collagen. Lung function showed there was a significant resistance in WT mice comparing with CKO mice.
Conclution: Our analysis shows that a knockout myocd in ASM can alters the architecture of the airway wall, decreases the hypertrophy, hyperplasia and proliferation of ASM, leading to reduced the numbers of proliferative inflamation cells, mucous secretion and the resistance of lung.

关键字 Myocardin; ASM; Remodeling; Asthma

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A survey on physical activity in children with asthma aged 6-17 years

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2. 国家儿童医学中心，首都医科大学附属北京儿童医院过敏反应科，国家呼吸系统疾病临床医学研究中心

Objective: To assess the difference of daily activity level between children with asthma aged 6-17 years and children without asthma aged 6-17 years, and to explore the relationship between physical activity level, asthma control and quality of life in children with asthma, this study summarizes the favorite exercise type of children with asthma and the attitude of their parents to the regular exercise training in children with asthma.

Methods: Children aged 6-17 years with confirmed asthma and children in same age without asthma were included as control group. The children in the asthma group came from the patients who were using the electronic version of CCAAP related mobile application for asthma self-management, and were followed up regularly in the outpatient clinic of the research center. The parents of children with asthma， were included in the study, who had established we-chat contact with the researchers. The control group was matched with the asthma group in age and gender and region. The questionnaire was designed in October 2019. In December 2020, the questionnaire was released online. Daily physical activities and sedentary behavior, asthma control, quality of life, favorite sports of children with asthma and parents' views on sports were assessed. Physical activity was assessed by the international physical activity questionnaire-short questionnaire, and the main indicator was the average time of moderate-to-vigorous physical activity (MVPA); sedentary behavior was assessed by the sedentary behavior section of the health behavior questionnaire for school-age children; asthma control was assessed by the ACT and c-ACT questionnaires; and quality of life was assessed by the scale of PedsQL 4.0. T test or rank sum test was used to compare the mean between the two groups, and variance analysis or rank sum test was used to compare the mean of multiple samples. Chi-square test or rank sum test was used to compare the ratio of two or more groups. When $P < 0.05$, there was significant difference among groups.

Results: A total of 272 questionnaires were collected. After screening, 217 valid questionnaires were saved, including 168 in asthma group and 49 in control group. The average time of MVPA (min/d) in asthma group was shorter than that in control group (16.0 ± 10.9 min/d)($P<0.05$) . In asthma group, the percentage of children in sedentary time more than 2 hours on Monday to Friday (77.4%) was higher than in the control group (59.2%) ($P <0.05$) , physical activity level in the asthma controlled group was higher than in the asthma uncontrolled group, in different asthma controlled groups, the mean time of MVPA (min/d) per day (8.6 min/d) in asthma controlled group was longer ($P<0.05$) than in the asthma uncontrolled group (5 min/d) ($P<0.05$) ; the score of PedsQL4.0 (role function) in asthma controlled group was higher (70 points) ($P<0.05$) than in asthma uncontrolled group (65 points). In the different physical activity level groups, PedsQL score (society function aspect) (90 point) of children with asthma in high activity level was higher than that of children with asthma in moderate activity level (85 point) or low activity level (75 point) ($P<0.05$). The favorite sport type of children with asthma is cycling, and 86.9%（146/168） parents of children with asthma was intended to participate in regular exercise training.

Conclusion: Children with asthma in 6 to 17 years have less physical activity and longer sedentary time. In addition, the increase of physical activity level has benefits for the improvement of quality of life and the level of asthma control; parents want children with asthma to have regular exercise training. Therefore, active physical activity should be encouraged in children with asthma.

关键字 children; asthma; physical activity; sedentary behavior

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A comparative evaluation of efficacy of inhaled budesonide and mometasone in Chinese children with mild persistent asthma: A single-blind, randomized study

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Abstract
Objective: A very limited options inhalational corticosteroids (ICS) are approved for pediatric use in China. Due to lack of consensus on which is the best ICS based treatment option to manage mild persistent asthma in children, we conducted the present study.
Methods: A single-centre, randomized, parallel-group, single-blind study was conducted in asthmatic children aged between 6-11 years. Budesonide (BUD) and mometasone furoate (MF) were administered as per approved dosing regimen using pressurized metered dose inhalers via oral inhalation route for a period of 12-weeks. The study outcome was assessed in terms of FEV1, symptom scores and non-occurrence of side effects.
Results: Among the 77 randomized asthmatic children, 71 completed the study protocol and were used in carrying out the analysis. The improvement of spirometric parameters like FEV1, FEV1/FVC and PEF values observed in MF group was significantly ($p<0.05$) greater than BUD group. Both treatments were well tolerated throughout 12-weeks of the study.
Conclusions: Although both drugs showed improvement in quality of life of asthmatic children, the improvement was augmented in MF treated children. Owing to low dosing frequency, MF could provide better treatment approach than BUD due to improved patient compliance.

关键字 Children、Mild Persistent Asthma、Budesonide、Mometasone

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Long noncoding RNA LINC-PINT retards the abnormal growth of airway smooth muscle cells via regulating the microRNA-26a-5p/PTEN axis in asthma

高沛*、丁颖、尹冰如、顾浩翔
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Abstract
Objective: Asthma is a chronic respiratory disease worldwide. This study aimed to explore the functions of the long noncoding RNA LINC-PINT (LINC-PINT) in asthma and the underlying molecular mechanism.
Methods: Rat asthma model was developed with ovalbumin sensitization and challenge. The serum IgE level, airway hyperresponsiveness (AHR), airway inflammation, and lung pathological changes of rats were evaluated. Airway smooth muscle cells (ASMCs) were stimulated with platelet-derived growth factor-BB (PDGF-BB) to mimic the asthma-like condition in cellular level. QRT-PCR was performed to examine the expression of LINC-PINT, microRNA-26a-5p (miR-26a-5p), and PTEN. MTT and transwell assays were performed to analyse the viability and migration of ASMCs. The protein expression of airway remodelling marker MMP-1 and MMP-9 was measured by western blot. The interactions among LINC-PINT, miR-26a-5p, and PTEN were assessed.
Results: The expression of LINC-PINT and PTEN was inhibited, while miR-26a-5p expression was enhanced in PDGF-BB-stimulated ASMCs. In vivo, LINC-PINT overexpression considerably decreased the serum IgE level, AHR, airway inflammation, and lung pathological changes in asthma rat model. In vitro, LINC-PINT up-regulation evidently inhibited the viability, migration, and MMP-1 and MMP-9 protein expression in PDGF-BB-stimulated ASMCs. Dual-luciferase reporter assay discovered that LINC-PINT targeted miR-26a-5p, and miR-26a-5p targeted PTEN in ASMCs. Feedback approaches proclaimed that miR-26a-5p overexpression or PTEN deficiency effectively reversed the suppressive effect of LINC-PINT overexpression on the abnormal growth of ASMCs in asthma.
Conclusions: LINC-PINT overexpression retarded the abnormal growth of ASMCs by down-regulating miR-26a-5p expression and up-regulating PTEN expression in asthma, offering a potential therapeutic target for asthma.

关键字 Asthma、LINC-PINT、microRNA-26a-5p/PTEN、Airway Smooth Muscle Cells

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CircEXOC5 acts through the PTBP1/Skp2/Runx2 axis to activate autophagy and promote acute lung injury

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AbstractBackground: Acute lung injury (ALI) remains a life-threatening condition associated with high mortality. To understand the pathogenesis of ALI, we focused on circEXOC5, a significantly up-regulated circRNA in ALI identified from a previous study, and examined its biological functions as well as molecular mechanisms in ALI development.
Methods: Using the in vivo cecal ligation and puncture (CLP)-induced ALI mouse model and in vitro lipopolysaccharide (LPS)-challenged mouse pulmonary microvascular endothelial cells (MPVECs), we examined the impacts of knocking down circEXOC5 (shEXOC5) on lung injury (by HE staining), inflammation (by measuring cytokine productions and immune cells in BAF), and autophagy (by quantifying autophagosomes and expressions of autophagy markers). The regulations between circEXOC5, PTBP1, Skp2, and Runx2 were investigated by combining bioinformatics analysis, RIP, RNA pull-down, luciferase assay, qRT-PCR, mRNA stability, and ubiquitination assays. The significance of Runx2 in shcircEXOC5-induced ALI phenotypes was examined both in vitro and in vivo.
Results: CircEXOC5 was significantly up-regulated and associated with increased inflammation and activated autophagy in CLP-induced ALI lung tissues as well as in LPS-challenged MPVECs. Knockdown of circEXOC5 markedly alleviated ALI injuries, inflammation, and activation of autophagy. Through the interaction with PBTP1, an RNA-binding protein, circEXOC5 accelerated the degradation of Skp2 mRNA, an E3 ubiquitin ligase for Runx2, and therefore increased Runx2 expression. Functionally, overexpressing Runx2 reversed shcircEXOC5-inhibited ALI injury, inflammation, or autophagy.
Conclusions: The signaling cascade circEXOC5/PTBP1/Skp2/Runx2, by essentially regulating inflammation and autophagy in at least MPVECs, aggravates sepsis-induced ALI. Therefore, targeting individual components of this axis may benefit the treatment of ALI.

关键字 Acute Lung Injury、Autophagy、CircEXOC5、PTBP1/Skp2/Runx2

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Clinical observation of rivaroxaban in the treatment of refractory pulmonary

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Background: To investigate the efficacy and safety of direct oral anticoagulants (DOACs) rivaroxaban in the treatment of refractory pulmonary embolism in children.

Method: The diagnosis and treatment of three pediatric cases of refractory pulmonary embolism were analyzed retrospectively. Case 1: A 11-year-old boy was admitted to hospital for "fever and cough for 9 days". Bronchoalveolar lavage fluid examination showed that the drug-resistant mutation site of Mycoplasma pneumoniae was positive for 2063A > G or 2064 A > g.He was diagnosed as "severe refractory mycoplasma pneumoniae and pleural effusion". three days after admission, he had left chest pain and rusty sputum. CTPA examination showed bilateral pulmonary embolism. Due to the influence of COVID-2019 epidemic, the patient could not continue to be hospitalized for regulating blood coagulation function. He had to accept subcutaneous injection of enoxaparin. After 3 months of subcutaneous injection of enoxaparin after discharge, the CTPA showed that the scope of bilateral pulmonary embolism was smaller than before. The treatment was changed to rivaroxaban 5 mg, twice a day for three more months. Case 2: A 10-year-old boy was admitted because of chest and upper left abdomen pain, hemoptysis, and fever during the COVID-2019 pandemic. CTPA showed multiple pulmonary artery emboli in both inferior lobes. ultrasound examination of abdominal blood vessels revealed thrombosis of the inferior vena cava. He was diagnosed as hereditary protein S deficiency based on the low activity protein S and protein C, a heterozygous deletion in PROS1 gene and A history of paternal thrombus. Although he improved partially from local use of urokinase by DSA. The boy did not responded well to warfarin prescribed in another hospital. Thus, Urokinase and LMWH were switched to rivaroxaban (10 mg in the morning and 5 mg in the evening) after acute stage in our hospital. PE was cured at 3 months follow-up.Life-long anticoagulation treatment was recommended. Case 3: An 8-year-old boy was admitted to hospital for "fever and cough for 4 days". Chest X-ray showed atelectasis and pleural effusion, while the SPO2 was 90% - 95%. The coagulation function was normal and no elevated D-dimer was measured. Bronchoscopy showed plastic sputum. However, the SPO2 was still low by percutaneous method after bronchoscopy treatmen without fever, chest pain or hemoptysis. CTPA showed embolisms in partial branch of right pulmonary artery. The children were treated with enoxaparin subcutaneously for 2 weeks and levofloxacin intravenously for 7days. When the condition was stable, the therapy transfered to rivaroxaban(5 mg bid) and levofloxacin orally.

Results: Case 1: After oral rivaroxaban for 3 months, CTPA reexamination showed the right pulmonary artery embolism recovered, and the left pulmonary artery embolism was narrowed. Rivaroxaban was given orally again for three months. He took it orally for totally six months. Case 2: His pulmonary embolism was cured, and the inferior vena cava below the renal vein level had recanalized at 3 months follow-up. Case 3:Two months after discharge, CTPA was reexamined and pulmonary embolism was cured.The three children were well tolerated during oral rivaroxaban, and no bleeding related adverse reactions occurred. However, Case 1 was unable to take medicine in time due to COVID-2019 epidemic situation, and left sequelae in follow-up.

Conclusions: With the increase of pulmonary embolism in children, heparin and warfarin are widely used in children. But they are inconvenient for children because of their medication route and the need for frequent blood collection to monitor anticoagulant activity. New oral anticoagulant drugs such as DOACs have stronger activity and do not need frequent monitoring. If they can be used early, the patient may benefit more. Therefore, Rivaroxaban may be an anticoagulation choice in children. It needs more clinical data support.

关键字 DOACs, pulmonary embolism; children

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Associations of fine particulate matter and constituents with pediatric emergency room visits for respiratory diseases in Shanghai, China

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Background: Although ambient fine particulate matter (PM2.5) has been associated with adverse respiratory outcomes in children, few studies have examined PM2.5 constituents with respiratory diseases in children in China. This study aimed to investigate the associations of short-term exposure to PM2.5 and its constituents with pediatric emergency room visits (ERVs) for respiratory diseases in Shanghai, China.
Methods: We collected daily concentrations of PM2.5 and its constituents in urban Shanghai from January 1,2016, to December 31, 2018. Daily mass concentrations of PM2.5 during the study period were calculated by averaging the daily means across ten fixed-site monitoring stations in the Shanghai National Air Quality Monitoring Network. Daily pediatric ERVs for four major respiratory diseases, including upper respiratory tract infection, bronchitis, pneumonia, and asthma, were obtained from 66 hospitals in Shanghai through electronic medical records during the same period. Associations of exposure to daily PM2.5 and constituents with respiratory ERVs were estimated using the over-dispersed generalized additive models.
Result: Short-term exposure to PM2.5 and its constituents were associated with increased pediatric ERVs for respiratory diseases. Specifically, an interquartile range increase in the 3-day average PM2.5 level (31 μg/m3) was associated with 1.86% (95%CI: 0.52, 3.22), 1.53% (95%CI: 0.01, 3.08), 1.90% (95%CI: 0.30, 3.52), and 2.67% (95%CI: 0.70, 4.68) increase of upper respiratory tract infection, bronchitis, pneumonia, and asthma ERVs, respectively. As for PM2.5 constituents, we found organic carbon, ammonium, nitrate, selenium, and zinc were associated with higher risk of respiratory ERVs in the single constituent and the constituent-PM2.5 models.
Conclusion: Short-term exposure to PM2.5 was associated with increased pediatric ERVs for respiratory diseases. Constituents related to anthropogenic combustion and traffic might be the dominant contributors of the observed associations.

关键字 PM2.5 constituents; Pediatric emergency room visits; Respiratory diseases

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Evaluation of the role of Dermatophagoides farinae drops sublingual immunotherapy in the treatment of allergic asthma in children

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Abstract
Background. Allergic asthma (AA) is the most common chronic respiratory disease in children, and allergen-specific immunotherapy (AIT) is considered to be the only possible cure for AA. Few Studies investigated the impact of AIT on airway inflammation and obstruction.
Methods. 133 AA children with Dermatophagoides sensitization were randomly assigned to observation group received Dermatophagoides farinae (D.farinae) drops sublingual immunotherapy (SLIT) combined with pharmacotherapy and control group received pharmacotherapy alone from outpatient department of Chengdu Women's and Children's Central Hospital from March 2017 to March 2019. We analyzed total rhinitis symptom scores (TRSS), total asthma symptom scores of daytime (DASS), total asthma symptom scores of night (NASS), total medication score (TMS), fractional exhaled nitric oxide (FeNO), forced vital capacity (FVC), forced expiratory volume in one second (FEV1), peak expiratory flow (PEF), forced expiratory flow at 50% and 75% of the FVC (FEF50 and FEF75), and maximum mid-expiratory flow (MMEF) of the two groups before treatment and 12 months later.
Results. TRSS, DASS, NASS, TMS, FeNO, FVC, FEV1, PEF, FEF50, FEF75 and MMEF of both groups significantly improved than baseline ($P < 0.05$), while the improvements of TRSS, DASS, NASS, TMS, FeNO, FEF50, FEF75 and MMEF of observation group were more obvious than control ($P < 0.05$).
Conclusion. D.farinae drops SLIT could better improve the symptoms of asthma and rhinitis, reduce medication use, and especially better improve airway inflammation and small airway disfunction of AA in children.

关键字 Allergic asthma, allergen-specific immunotherapy, randomized controlled trial, children

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Clinical analysis of 42 children with bronchiectasis

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Objective：The clinical data of 42 cases of children bronchiectasis were analyzed in order to improve the understanding of children bronchiectasis and to achieve the purpose of early diagnosis and treatment.Methods：
Clinical data of 42 children with bronchiectasis aged 0-14 years who were hospitalized in the Affiliated Hospital of Guizhou Medical University from January 2015 to February 2021 were collected, including 29 males and 13 females.The general data , clinical data , laboratory data , the other inspection data , fiberoptic bronchoscopy lung function, treatment and outcome were retrospectively analyzed.SPSS21.0 software was used for statistical analysis of the data. counting data were expressed as rate or percentage (%).Univariate analyses or inter-group comparisons were performed using Fisher's exact test.Results:1.42 children with bronchiectasis, including 29 males and 13 females, had a male to female ratio of 2.23:1.Most of the patients (18 cases, 42.9) had > at 4 weeks,.2. Infection was the most common cause in this study, with 22 cases (52.3);The other 20 non-infected cases .3. Among the clinical manifestations of bronchiectasis in children, cough, sputum and fever are the most common, while wheezing, hemoptysis, backward growth and development and anemia are less common.The most common clinical signs were persistent wet rales (including phlegm) in 26 cases (61.9 cases).4. Etiological statistics showed that there were 16 cases of mycoplasma pneumoniae infection (38.1), 13 cases of bacterial infection, 10 cases of viral infection, 4 cases of tuberculosis bacilli infection and 2 cases of fungal infection.The results of bacterial culture were statistically analyzed. Among the 42 children, 39 cases were submitted for culture, with a rate of 92.9. A total of 100 samples were submitted, and 21 strains of bacteria were detected (positive rate was 21.0).5. Chest CT examination was performed in all 42 children, with a positive rate of 100.0;bilateral lung involvement was the most common, with a total of 23 cases (54.8).The distribution of different types of bronchiectasis in children with bronchiectasis was statistically analyzed. 7. A total of 6 patients underwent bronchial examination, among which inflammation and purulent secretions of trachea and endobronchial membrane, foreign body in 1 case, mucus embolus in 2 cases, mucosal tuberculosis in 1 case, and bronchial lumen dilatation and stenosis in 1 case were found in all the 6 patients.8. All 42 children in this study were treated with antibiotics empirically or according to the results of etiological examination, 7 with antiviral therapy, 2 with antifungal therapy, 4 with antituberculous therapy, 4 with lobotomy and 3 with removal of bronchial foreign body;9. In this study, 25 cases were cured and discharged, 9 cases were better and discharged, 7 cases were discharged without medical advice, and 1 case of congenital immunodeficiency died .Conclusions：1. Infection is still the most common cause of bronchiectasis in children, followed by immunodeficiency, foreign body inhalation, asthma, etc. 2.The clinical manifestations of children with bronchiectasis are lack of specificity,but cough, sputum, fever and wheezing are the most common manifestations. 3.In the 42 children with bronchiectasis in this study, the most common pathogen was Mycoplasma pneumoniae, followed by bacteria, viruses, Mycobacterium tuberculosis and fungi, which has certain guiding significance for the selection of antibiotics. 4.With the use of HRCT, it has gradually replaced bronchography as the gold standard for the diagnosis of bronchiectasis in children, and HRCT can indicate the type and range of bronchiectasis, which is of great

significance for the search for etiology and treatment. 5.The treatment of bronchiectasis can be divided into symptomatic treatment and causative treatment. The therapeutic effect and outcome of bronchiectasis are related to the underlying etiology.

关键字 Children;Bronchiectasis, Etiology, CT, Infection

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A preliminary study on the characteristics of clinical data in children with community acquired pneumonia and the establishmalet of deep learning clinical model

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Objective: To analyze the overall clinical data characteristics of community-acquired pneumonia(CAP) in children in a single center, and to establish a clinical model based on serum C-reactive protein (CRP) and white blood cell (WBC) count, and to explore the value of the model in distinguishing viral pneumonia, bacterial pneumonia and mycoplasma pneumonia.
Methods: The clinical data of hospitalized patients with communityacquired pneumonia diagnosed from January 2011 to December 2018 were collected, including age, gender, admission time, course of disease, main and secondary diagnosis, etiological diagnosis, basic disease and other basic information.Meanwhile, 1769cases of hospitalizedchildren with communityacquired pneumonia in our hospital from 2013 to 2018 were collected, including 487 cases of viral pneumonia, 496 cases of bacterial pneumonia and 786 cases of mycoplasma pneumonia. CRP, WBC count and basic information of children with three kinds of pneumonia were collected, and the samples were divided into training set, verification set and test set according to 7:1:2. Through these two clinical indicators to establish a clinical model, determine the accuracy of the model in the diagnosis of different pathogens of pneumonia, and train the clinical model to obtain the best diagnostic efficiency.
Results: A total of 19873 hospitalized children were included from 2011 to 2018, with the most hospitalized cases of pneumonia in infancy (41.63%) and the least hospitalized cases in adolescence (4.4%). Mycoplasma pneumonia was the most common single infection (41.1%), followed by bacterial pneumonia (16.23%). The detection rate of mycoplasma pneumonia in female was higher than that in male (P< 0.001), and the difference was statistically significant. The detection rate of viral pneumonia and bacterial pneumonia in male was higher than that in female (P< 0.001). The seasonal distribution of different pathogenic pneumonia was also different. Mycoplasma pneumonia was more common in autumn and winter, while viral pneumonia and bacterial pneumonia were mainly concentrated in winter, and the difference was statistically significant (P < 0.001).Mycoplasma pneumonia was more common in school age, followed by preschool age (P< 0.001); viral pneumonia was more common in infants and young children, and the virus detection rate showed a downward trend with age (P< 0.001); bacterial pneumonia was more common in infants and young children. From 2011 to 2018, the detection rate of mycoplasma pneumonia had two small peaks, the detection rate of viral pneumonia increased slightly, the detection rate of bacterial pneumonia decreased slightly, and the detection rate of other pathogenic pneumonia was stable. The positive rates of CRP and WBC in children with different pathogenic pneumonia were statistically significant (P< 0.001). The clinical model had diagnostic value for pneumonia with different pathogen, but the diagnostic efficiency was poor. The ACC of the model in the training set was 0.60, and that in the test set was 0.51.Forviral pneumonia the area under the curve of the model in the training set was 0.665, and that in the test set was 0.619. Forviral pneumonia, the

area of under the curve in the training set was 0.699, and 0.605 in the test set. Formycoplasma pneumonia, the area of under the curve in the training set was 0.70, and 0.654 in the test set.
Conclusion: Mycoplasma is the main pathogen of children's communityacquired pneumonia. Children with mycoplasma pneumonia mainly concentrated in school age and pre-school age. The detection rate of mycoplasma pneumonia in female was higher than that in male. The detection rate of viral pneumonia and bacterial pneumonia in male was higher than that in female. CRP, WBC data training clinical model, clinical model has diagnostic value for detecting three kinds of pathogenic pneumonia, mycoplasma pneumonia detection efficiency is the highest.

关键字 community acquired pneumonia, children, epidemiology, machine learning

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Exploring the role of basophil activation test in diagnosis of Derf sensitization and evaluation of therapeutic efficacy of subcutaneous immunotherapy in children

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Objective:

It aims to detect basophil activation ratio (%$CD63^+$) in peripheral blood of children with allergic asthma and rhinitis by using Flow cytometry (FCM) , so as to analyze the application values and clinical relevance of the Basophil Activation Test (BAT) in diagnosis of dermatophagoides farinae sensitization and monitoring therapeutic efficacy of subcutaneous immunotherapy (SCIT).

Methods:

It was a prospective study. We enrolled the children who attended the pediatric asthma clinic in the Second Hospital of Tianjin Medical University from October, 2018 to May, 2019. From the newly diagnosed children with asthma and rhinitis, 22 patients diagnosed Derf sensitization were enrolled as sensitization group; 7 patients not allergic to Derf were enrolled as non-sensitized group; another 4 healthy children were taken as the normal control group. Using Derf extracts in the concentration of 1 μg/ml, 10 μg/ml and 100 μg/ml as the stimulus , basophils were obtained by the gates CD123 and HLA-DR. %$CD63^+$ measured by FCM was used to evaluate BAT in the diagnosis of Derf sensitization and its correlation with skin prick tests (SPT), serum total IgE (TIgE), specific IgE (sIgE), sIgE / TIgE, specific IgG4 (sIgG4), FEV1%pred in pulmonary ventilation function, exhaled nitric oxide (FeNO), children asthma control test (C-ACT) and visual analogue scale (VAS). In sensitization group, 15 patients who had received standardized SCIT for 6 months were detected %$CD63^+$, sIgG4 and clinical indicators again to analyze their internal connections.

Results:

1. Comparison of basophil activation ratios in different concentrations in sensitization group

The optimal stimulating concentration of dust mites was 100 μg/ml. The average levels of %$CD63^+$ in the concentrations of 1μg/ml, 10μg/ml and 100μg/ml showed an increasing concentration-dependent trend overall. The %$CD63^+$ in the concentration of 100 μg/ml in a small number of individuals were lower than the former (10 μg/ml).

2. Comparison of basophil activation ratios in different groups

%$CD63^+$ in sensitization group was significantly higher than that in the other two groups ($p < 0.05$).

3. Diagnostic value of Derf sensitization between basophil activation ratio and sIgE

SPT regarded as the gold standard, the analysis of ROC for Derf sensitization showed that the area under the curve (AUC) for BAT in three concentrations (0.992、0.967、0.930) were higher than that for sIgE whose AUC was 0.893. Its sensitivity and specificity in three concentrations were 77.3%,100%; 81.8%,100%; 72.7%,91%, respectively. Among the BAT results, 3 cases were false positive results, accounting for 9.1%; 2 cases were false negative results, accounting for 6.1%.

4. The correlation between clinical indicators and basophil activation ratio
There was a positive correlation between %CD63^{+} and SPT grade in Spearman rank correlation analysis. %CD63^{+} was positively correlated with sIgE, sIgE / TIgE and VAS, and negatively correlated with C-ACT in Pearson linear correlation analysis. %CD63^{+} was not correlated with TIgE, FEV1%pred and FeNO.
5. The change of basophil activation ratio, sIgG4, sIgE/sIgG4, sIgE/TIgE and clinical indicators before and after SCIT
In sensitization group, %CD63^{+} in three concentrations , sIgE/sIgG4 and VAS from 15 patients after SCIT were lower than before. The average level of sIgG4 and C-ACT became higher than before. There was no significant difference in sIgE/TIgE. There was no obvious change in sIgG4 in those who hadn't received SCIT.
Conclusions:
1. BAT is a safe and effective method in vitro for diagnosing Derf sensitization in children with asthma and rhinitis, and has good clinical relevance in assessing the severity of symptoms.
2. The symptoms of children with asthma and rhinitis improved after standardized SCIT (6 months). BAT and sIgG4 can be used as biomarkers to evaluate the efficacy of SCIT and the change of basophil activation ratio is intrinsically related to the induction of sIgG4.

关键字 Basophil activation test, Dermatophagoides farinae, Allergic disease, Diagnosis, Treatment, Flow cytometry, Children

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Exploring the role of different biomarkers in evaluation and prediction of therapeutic efficacy of subcutaneous immunotherapy in children with Derf sensitization

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Objective:
It aims to detect the change of basophil activation ratio (%$CD63^+$) in peripheral blood, serum specific IgE (sIgE), total IgE (TIgE), sIgE/TIgE and specific IgG4 (sIgG4) in children with allergic asthma and rhinitis sensitized by dermatophagoides farina (Derf) after receiving subcutaneous immunotherapy (SCIT), so as to analyze the application values and clinical relevance of above indicators in evaluation and prediction of SCIT therapeutic efficacy.

Methods:
It was a prospective study. We enrolled the children who attended the pediatric asthma clinic in the Second Hospital of Tianjin Medical University from May, 2018 to May, 2019. A total of 42 children who were newly diagnosed as asthma and rhinitis sensitized by Derf were selected and accepted conventional treatment. Among them, 35 patients received standardized SCIT (SCIT group) and 7 patients received only conventional treatment (control group). Using Derf extracts in the concentration of 1 μg/ml, 10 μg/ml and 100 μg/ml as the stimulus, basophils were obtained by the gates CD123 and HLA-DR. %$CD63^+$ measured by Basophil Activation Test (BAT), the serum immunological indexes (sIgE, TIgE, sIgE/TIgE and sIgG4), children asthma control test (C-ACT) and visual analogue scale (VAS) were detected before and after 52 weeks of SCIT in two groups and their internal connections were analyzed. The SCIT group was divided into effective group and ineffective group according to the improvement of symptom scores after 52 weeks.

Results:
1. sIgE/TIgE level at baseline: Taking symptom scores improvement as the gold standard, 25 cases were effective and 10 cases were ineffective in SCIT group. Receiver operating characteristic (ROC) curve analysis showed that the area under the curve (AUC) for sIgE/TIgE was higher than that for sIgE and TIgE, suggesting sIgE/TIgE at baseline had the best predictive effect on SCIT therapeutic efficacy, whose cut-off value was 21.7%, and the sensitivity and specificity were 86.2% and 77.6%, respectively.
2. %$CD63^+$: The optimal stimulating concentration of Derf was 100 μg/ml. There was no significant difference in %$CD63^+$ between effective group and ineffective group before treatment ($P>0.05$). In effective group, the average level of %$CD63^+$ after SCIT was lower than before; %$CD63^+$ level in effective group was lower than that in ineffective group after treatment ($P<0.05$). There was a positive correlation between %$CD63^+$ and SPT grade before treatment in Spearman rank correlation analysis ($p<0.05$); Pearson linear correlation analysis showed that %$CD63^+$ after treatment was positively correlated with rhinitis VAS, and negatively correlated with C-ACT and baseline sIgE/TIgE ($p<0.05$). %$CD63^+$ was not correlated with sIgE and TIgE ($P>0.05$).
3. sIgG4: There was no significant difference in sIgG4 between the effective group and ineffective group before treatment ($P>0.05$). After treatment, sIgG4 in two groups

were higher than before (P<0.05), and there was no significant difference between the two groups after treatment (P>0.05); sIgG4 in control group had no obvious change before and after treatment (P>0.05). There was no exact correlation between the quantitative level of sIgG4 and clinical efficacy (P>0.05).

Conclusions:

1. The level of sIgE/TIgE at baseline can be used as a predictor of clinical improvement of SCIT, and those with a larger ratio are more likely to obtain satisfactory results.
2. %$CD63^+$ can be used as a biomarker to evaluate the efficacy of SCIT, and it has good clinical relevance in assessing the severity of symptoms.
3. The change of sIgG4 reflects compliance, and the change of %CD63+ is intrinsically related to the induction of sIgG4.

关键字 Biomarker, Basophil activation test, Subcutaneous immunotherapy, Children

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Plasma TNFSF13B and TNFSF14 Function as Inflammatory Indicators of Severe Adenovirus Pneumonia in Pediatric Patient

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Background: Human adenoviruses (HAdV) infection caused pneumonia remains a major threat to global children health. Currently, diagnosis of severe HAdV pneumonia in children is hampered by the lack of specific biomarkers. Also, the severity of adenovirus pneumonia in pediatric patients is generally based on clinical features and existing biomarkers do not reliably correlate to clinical severity. Here, we asked whether local and systemic inflammatory mediators could act as biomarkers predicting severe HAdV pneumonia in children.
Methods: Totally 37 common inflammatory protein levels were determined by Luminex assay in plasma and bronchoalveolar lavage (BAL) from pediatric patients who were diagnosed with HAdV pneumonia, and their correlation with the disease severity and lung lesion were assessed using statistical and bioinformatic analysis.
Results: Among 37 inflammatory cytokines, the protein levels of 4 TNF superfamily (TNFSF) members and their receptors (TNF receptor superfamily, TNFRSF) [TNFSF13B, TNFSF14, sTNF-R1 and sTNF-R2] in the plasma and 7 TNFSF/TNFRSF members [TNFSF12, TNFSF13, TNFSF13B, TNFSF14, TNFRSF8, sTNF-R1, and sTNF-R2] in the BAL were enhanced in patients with HAdV pneumonia compared with control subjects
with airway foreign body. Moreover, the protein levels of all the tested TNFSF/TNFRSF members (except TNFSF12) were elevated in the BAL of severe group compared with non-severe HAdV pneumonia patients, while only TNFSF13B and TNFSF14 were dramatically increased in the plasma of severe cases, and positively related to the plasma CRP levels. In addition, ROC analysis indicated that TNFSF13B and TNFSF14 displayed a great potential to predict severe HAdV pneumonia.
Conclusion: In pediatric HAdV pneumonia, TNFSF/TNFRSF members function as key molecules in local and systemic inflammatory network, and the plasma TNFSF13B and TNFSF14 may be the potential local and systemic inflammatory indicators of severe HAdV pneumonia in pediatric patients.

关键字 tumor necrosis factor receptor superfamily (TNFRSF), adenovirus, pediatric, pneumonia, inflammation

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Frequency of asthma exacerbation in children during the coronavirus disease pandemic with strict mitigative countermeasures

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Background: Strict countermeasures for coronavirus disease (COVID‐19) were undertaken in China without knowing their influence on asthma.
Objective: To investigate the associations between the frequencies of asthma exacerbations and respiratory infections and air pollutants before and during the COVID‐19 pandemic, which were direct consequences of countermeasures undertaken for the pandemic.
Methods: Asthma exacerbations and respiratory infections among hospitalized children in the permanent population of Guangzhou City, China, from February to June 2016‐2019 (before the pandemic) to February to June 2020 (during the pandemic) were collected in this cross‐sectional study in Guangzhou.
Results: The number of asthma exacerbation cases per month documented in the Guangzhou Women and Children's Hospital before (median: 13.5; range: 0‐48) and during (median: 20; range: 0‐34) the mitigative response to the COVID‐19 pandemic was similar. The frequency of severe asthma exacerbation cases per month decreased, whereas that of mild asthma exacerbation cases per year increased (p = .004). The number of patients hospitalized with infectious respiratory diseases decreased from 146 (range: 90‐172) per month before the pandemic to 42 (range: 33‐57) per month during the pandemic (p = .004). Most pathogens and air pollutants decreased during the COVID‐19 pandemic. The frequency of severe asthma exacerbations positively correlated to that of respiratory infections in children, but did not correlate to air pollutants.
Conclusion: Strict countermeasures undertaken for the pandemic were associated with a decreased the frequency of infectious respiratory diseases and severe asthma exacerbations among urban children.

关键字 air pollution, asthma exacerbation, COVID‐19, prevention, respiratory infection

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Early prediction of the severity of lung necrosis in children’s community-acquired necrotizing pneumonia

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Objective:The aim of the present study was to analyze the clinical and laboratory characteristics at baseline and explore the possible predictors of the severity of lung necrosis in children’s community-acquired necrotizing pneumonia.
Methods:This study was conducted retrospectively in a tertiary referral center. We searched the computer-based database for CAP patients under 15 years of age who had been interpreted radiologically as “necrotizing pneumonia”. Patients were allocated into mild ,moderate or massive necrosis groups, and they were compared with respect to various clinical variables.
Results: A total of 104 patients with a diagnosis of community-acquired NP were enrolled in this study.29 cases were with mild necrosis,41 with moderate necrosis, 34 cases with massive necrosis. The cases with massive necrosis were much more likely to occur in winter(P＜0.05)and they exhibited more severe clinical outcomes，such as longer fever days, longer hospital stay, a higher risk of requiring subsequent surgical intervention and mortality (P＜0.05)(Table 1). Multivariate analysis showed that CRP≥122mg/L(aOR 8.780 and 95% CI 3.320－21.089; p = 0.003) ,serum albumin ≤30.8g/L (aOR 11.608 and 95% CI 5.147－27.058; p = 0.001), IgM≤95.7mg/dl (aOR 7.152 and 95% CI 2.240－17.692; p = 0.031)were independent risk factors for massive necrosis. They showed good diagnostic performance for differentiating cases with massive necrosis from all NP patients by ROC curves analysis.

Conclusion: NP is a potentially severe complication of community-acquired pneumonia in children.Different degrees of pulmonary necrosis can lead to different clinical outcomes.The levels of CRP,serum albumin and IgM are independent predictors of degree of pulmonary necrosis.

关键字 necrotizing pneumonia，children，predictor，degree of lung necrosis

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Etiological Distribution and changes of single center plastic bronchitis in Shenzhen Children's Hospital from 2010 to 2019

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Objective To investigate the etiological distribution and changes of pediatric plastic bronchitis (PB) in a single center of Shenzhen Children's Hospital from 2010 to 2019, and to provide reference for further improving the understanding of the etiology of PB.
Methods The clinical data of children diagnosed with PB in Shenzhen Children's Hospital from 2010 to 2019 were retrospectively analyzed, and the etiological distribution characteristics and changes were summarized.
Results There were 266 cases of PB in recent 10 years, including 164 males, 102 females, 16 infants, 60 infants, 115 preschoolers and 75 school-age children.Among 266 PB cases, 94 cases were mycoplasma pneumoniae, 38 cases were influenza virus, 41 cases were adenovirus, 19 cases were mixed infection, 8 cases were bacterial infection and 60 cases were unknown etiology.From 2010 to 2019, the positive detection rates of pathogens were 62.5%, 60.0%, 66.7%, 74.1%, 64.0%, 50.0%, 93.3%, 57.1%, 75.0%, 84.7%, respectively.From 2010 to 2019, mycoplasma pneumoniae was found in PB etiology every year, but adenovirus and mycoplasma pneumoniae accounted for significantly higher proportions in 2019.Among 266 PB cases, 115 cases were preschoolers, 60 cases were preschoolers and 75 cases were preschoolers, and only 16 cases were infants.
Conclusion The incidence of PB in children is increasing year by year, which is closely related to infection.The etiology of MP infection was the first, followed by adenovirus and influenza virus, and less bacteria, fungi and other viruses.In 2019, adenovirus and mycoplasma infection caused a significant increase in PB, which was related to the adenovirus outbreak in the region.

关键字 plastic bronchitis, children, etiology

分类：23. Pulmonology 呼吸
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Risk factors for mortality from severe community-acquired pneumonia in hospitalized children transferred to the pediatric intensive care unit

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Background: Some children hospitalized due to severe community-acquired pneumonia (CAP) require to the pediatric intensive care unit (PICU) because of severe complications. The purpose of this study was to identify the risk factors for mortality in this patient population.
Methods: This study evaluated the medical records of 113 hospitalized children with severe CAP, who were transferred to the PICU within 48 h of admission at the Guangzhou Women and Children's Medical Center between 2013 and 2017.
Results: The study group consisted of 87 boys (77%) and 26 girls (33%), aged between 1 month and 9 years; 72.6% (82/113) of patients were aged <12 months. The mortality rate was 12.3% (14/113). The most common viral and bacterial pathogens isolated were adenovirus (17.7%, 20/113) and Haemophilus influenzae (8.8%, 10/113). Wheezing, cyanosis, oxygen saturation <90%, Pediatric Early Warning Score (PEWS) >3 on admission, not receiving corticosteroid therapy prior to admission, the need for mechanical ventilation, septic shock, multi-organ dysfunction (MODS), and acute renal failure (ARF) occurring prior to transfer to the PICU, increased alanine aminotransferase (ALT) and aspartate transaminase (AST) levels, and decreased hemoglobin and albumin (ALB) levels were associated with mortality ($P < 0.05$). Non-survivors were more likely to have an oxygen saturation <90% on admission and lower levels of ALB prior to transfer to the PICU than survivors ($P < 0.05$).
Conclusions: Our results showed that hospitalized children with severe CAP who were transferred to the PICU within 48 h of hospital admission were mainly aged <1 year. Additionally, an oxygen saturation <90% and decreased ALB levels were early prognostic variables independently associated with death.

关键字 community-acquired pneumonia; hospitalized children; pediatric intensive care unit; risk factors

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Total and double-stranded DNA-specific immunoglobulin E in bronchoalveolar lavage fluid of children with human adenovirus pneumonia

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Background: Some antibodies and autoreactive antibodies are associated with the severity of infectious diseases. The roles of humoral responses to lung inflammation in children with human adenovirus (HAdVs) pneumonia remain unknown.
Patients and methods: A retrospective study was done to compare plasma immunoglobulin E (IgE) levels between HAdVs pneumonia patients and healthy children by searching the electronic medical record system of Guangzhou Women and Children's Medical Center. Then, a prospective study was performed for children with HAdVs pneumonia who needed flexible bronchoscopy for examination and treatment purposes during July 2017 to July 2019. We examined the IgE and autoreactive IgE levels in plasma and bronchoalveolar lavage fluid (BALF) of these children to explore their role in HAdVs pneumonia.
Results: A significantly higher level of IgE was found in plasma from children hospitalized with HAdVs pneumonia compared with that from healthy children in the same age range. Furthermore, the levels of IgE, double-stranded DNA (dsDNA), and double-stranded DNA-specific immunoglobulin E (dsDNA-IgE) in BALF were increased compared to plasma in children with HAdVs pneumonia. The levels of IgE, dsDNA, and dsDNA-IgE in BALF were significantly higher in the severe group compared to the non-severe group. The ability of IgE in BALF to recognize dsDNA was verified by the ELISPOT test.
Conclusions: Our findings indicate that IgE and dsDNA-IgE in BALF may contribute to lung injury caused by HAdVs, especially in severe cases. Elevated dsDNA-IgE may serve as an indicator of severity in children with HAdVs pneumonia.

关键字 Children; Double-stranded DNA; Human adenovirus pneumonia; Immunoglobulin E

分类：23. Pulmonology 呼吸
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Identification of miRNA-mRNA Crosstalk in Respiratory Syncytial Virus- (RSV-) Associated Pediatric Pneumonia through Integrated miRNAome and Transcriptome Analysis

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Respiratory syncytial virus (RSV) is the most common respiratory virus and is associated with pediatric pneumonia, causing bronchiolitis and significant mortality in infants and young children. MicroRNAs (miRNAs) are endogenous noncoding small RNAs that function in gene regulation and are associated with host immune response and disease progression. In the present study, we profiled the global transcriptome and miRNAome of whole blood samples from children with mild or severe RSV-associated pneumonia, aiming to identify the potential biomarkers and investigate the molecular mechanisms of severe RSV-associated pediatric pneumonia. We found that expression profiles of whole blood microRNAs and mRNAs were altered and distinctly different in children with severe RSV-associated pneumonia. In particular, the four most significantly upregulated miRNAs in children with severe RSV-associated pneumonia were hsa-miR-1271-5p, hsa-miR-10a-3p, hsa-miR-125b-5p, and hsa-miR-30b-3p. The severe RSV-associated pneumonia-specific differentially expressed miRNA target interaction network was also contrasted. These target genes were further analyzed with Gene Ontology enrichment analysis. We found that most of the target genes were involved in inflammatory and immune responses, including the NF-κB signaling pathway, the MAPK signaling pathway, and T cell receptor signaling. Our findings will contribute to the identification of biomarkers and new drug design strategies to treat severe RSV-associated pediatric pneumonia.

关键字 Respiratory Syncytial Virus; miRNA-mRNA Crosstalk; Pneumonia; Pediatric

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Pathogenic Fungal Infection in the Lung

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Respiratory fungal infection is a severe clinical problem, especially in patients with compromised immune functions. Aspergillus, Cryptococcus, Pneumocystis, and endemic fungi are major pulmonary fungal pathogens that are able to result in life-threatening invasive diseases. Growing data being reported have indicated that multiple cells and molecules orchestrate the host’ s response to a fungal infection in the lung. Upon fungal challenge, innate myeloid cells including macrophages, dendritic cells (DC), and recruited neutrophils establish the first line of defense through the phagocytosis and secretion of cytokines. Natural killer cells control the fungal expansion in the lung via the direct and indirect killing of invading organisms. Adaptive immune cells including Th1 and Th17 cells confer anti-fungal activity by producing their signature cytokines, interferon-γ, and IL-17. In addition, lung epithelial cells (LEC) also participate in the resistance against fungal infection by internalization, inflammatorycytokineproduction,or antimicrobialpeptidesecretion.Inthehostcellsmentionedabove,variousmoleculeswith distinct functions modulate the immune defense signaling: Pattern recognition receptors (PRRs) such as dectin-1 expressed on the cell surface are involved in fungal recognition; adaptor proteins such as MyD88 and TRAF6 are required for transduction of signals to the nucleus for transcriptional regulation; inflammasomes also play crucial roles in the host’s defense against a fungal infection in the lung. Furthermore, transcriptional factors modulate the transcriptions of a series of genes, especially those encoding cytokines and chemokines, which are predominant regulators in the infectious microenvironment, mediating the cellular and molecular immune responses against a fungal infection in the lung.

关键字 pulmonary fungal infection, pattern recognition receptor, inflammasome, cytokine, chemokine

分类：23. Pulmonology 呼吸
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Bronchoalveolar lavage with pediatric flexible fibreoptic bronchoscope in pediatric haematopoietic stem cell transplant patients: Nursing considerations for operative complications

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Purpose: Bronchoalveolar lavage (BAL) with pediatric flexible fibreoptic bronchoscopy (FB) is used for diagnostic and therapeutic purposes in pediatric haematopoietic stem cell transplant (HSCT) patients with pulmonary complications. The aim of our study was to evaluate complications in pediatric HSCT patients undergoing BAL/FB and to explore the nursing emphases on complications.
Design and Methods: We performed a retrospective, case-controlled study to evaluate perioperative complications of HSCT children. BAL/FB was conducted for 42 children with HSCT who experienced pulmonary complications between January 2017 and January 2018 within a tertiary hospital. 40 patients diagnosed with general pneumonia were randomly selected during the same period and served as the control group. We analysed the signs and symptoms of all patients and compared the operative complications between the two groups. Furthermore, we presented the methods used to manage complications.
Results: The presence of cough, lung rales and imaging findings in the HSCT patients was significantly different from that of the control group ($P<0.0001$). The complication rate was 66.67% (28/42) in the HSCT group and 22.5% (9/40) in the control group, and the difference was significant ($P<0.0001$). Twelve out of 42 HSCT patients experienced airway mucosal bleeding (28.57%), and 6 had transient fever (14.29%). The topical use of epinephrine diluted saline (1:10,000) was highly effective for controlling airway mucosal bleeding without causing fluctuations in blood pressure.
Practice Implications: There were more perioperative complications in the HSCT patients than in the general pneumonia patients who underwent BAL/FB. Airway mucosal bleeding was a key focus of perioperative nursing in HSCT patients undergoing bronchoscopy as main complication. BAL with the use of epinephrine diluted saline (1:10,000) effectively decreased airway mucosal bleeding.

关键字 haematopoietic stem cell transplant, bronchoalveolar lavage, bronchoscopy, pediatrics, complication

分类：23. Pulmonology 呼吸
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rRNA-depleted RNA sequencing reveals the pathogenesis of refractory Mycoplasma pneumoniae pneumonia in Children

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Pneumonia caused by Mycoplasma pneumoniae (MP) is the major cause of community-acquired pneumonia in children. In some cases, mycoplasma pneumoniae pneumonia (MPP) can develop into refractory MP pneumonia (RMPP), which shows no clinical or radiological response to macrolides, and can progress to severe and complicated pneumonia. However, the pathogenesis is still poorly understood. In the present study, we aimed to provide some target genes as the biomarkers for clinical diagnosis of RMPP in an early stage through a high-throughput sequencing technology. We compared the differences of lncRNAs, mRNAs and circRNAs between the whole blood samples from two non-refractory MP pneumonia (NRMPP) patients, two RMPP patients, and three healthy children with the rRNA-depleted RNA-sequencing techniques and the integrated mRNA-circRNA analysis. A total of 17 lncRNAs (4 up-regulated and 13 down-regulated), 18 mRNAs (6 up-regulated and 12 down-regulated), and 24 circRNAs (12 up-regulated and 12 down-regulated) were significantly altered ($P < 0.05$) in the NRMPP and RMPP comparative groups. Upon functional analysis, the significantly differentially expressed genes (DEG) encoded by the mRNA (PTGS2, IL-8, and FOSL1) were screened out and enriched in the IL-17 signaling pathway. Meanwhile, the key circRNAs in the NRMPP and RMPP comparative groups were mainly enriched in herpes simplex virus 1 infection, viral carcinogenesis, and RNA transport signaling pathways. In this study, a comprehensive analysis of the differences between the NRMPP and RMPP cases was performed based on the rRNA-depleted RNA-sequencing techniques, and the selected genes and circRNAs may be closely associated with the RMPP pathogenesis, which reflects the complex pathogenesis of RMPP.

关键字 Refractory mycoplasma pneumoniae pneumonia; rRNA-depleted RNA sequencing; lncRNA; circRNA

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Mortality risk factors in children with severe influenza virus infection admitted to the pediatric intensive care unit

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Some children hospitalized for severe influenza virus infection require intensive care or die because of disease progression, which may be combined with other complications. The objective of this study was to identify the mortality risk factors in the patients with severe influenza virus infection admitted to the pediatric intensive care unit (PICU).
Seventy-seven pediatric patients with severe influenza virus infection who were admitted in the PICU at Guangzhou Women and Children’s Medical Center between 2013 and 2017 were evaluated. Data were transcribed and analyzed.
The patients’ median age was 3.0 years (interquartile range, 1.0–4.0 years), with 59.7% of the patients aged <3 years. The mortality was 16.9%, and patients aged>3 years accounted for 69.2% of the cases. Influenza A virus infection was found in 83.1% of the patients. Coinfection was detected in 58.7% of the patients. Haemophilus influenzae (11.7%) and adenovirus (9.1%) were the predominant bacterial and viral pathogens isolated, respectively. Older age, oxygen saturation level of <90% at admission, acute respiratory distress syndrome, pneumorrhagia, influenza-associated encephalopathy (IEA), septic shock, low ratio of partial pressure of oxygen in arterial blood (PaO2, <60 mm Hg) to the fraction concentration of oxygen in inspired air (FiO2; P/F), higher oxygenation index, increased alanine aminotransferase level (>100IU/L), increased aspartate aminotransferase level (>100IU/L), increased lactate dehydrogenase level (>500IU/L), high fraction concentration of oxygen in inspired air (FiO2 > 60%), and positive endexpiratory pressure (>8cmH2O) were associated with poor outcome. The deceased patients were more likely to have oxygen saturation levels of <90% at admission and IEA than those who survived. Higher P/F ratio was a protective factor against death in patients.
The children with severe influenza virus infection who were admitted in the PICU were mainly aged <3 years. The presence of an oxygen saturation level of <90% at admission and IEA were the prognostic variables independently associated with mortality. Higher P/F ratio was a protective factor against death in patients.

关键字 children, influenza virus, pediatric intensive care unit, risk factor

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MicroRNA Expression Profile of Whole Blood Is Altered in Adenovirus-Infected Pneumonia Children

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Human adenovirus (Adv) infection is responsible for most community-acquired pneumonia in infants and children, which results in significant morbidity and mortality in children every year. MicroRNAs (miRNAs) are associated with viral replication and host immune response. Knowing the miRNA expression profile will help understand the role of miRNAs in modulating the host response to adenovirus infection and possibly improve the diagnosis of adenovirus-infected pneumonia. In our study, total RNA extracted from whole blood of adenovirus-infected pneumonia children and healthy controls were analyzed by small RNA deep sequencing. Expression profiles of whole blood microRNAs were altered and distinctly different in adenovirus-infected children. The top 3 upregulated miRNA (hsa-miR-127-3p, hsa-miR-493-5p, and hsa-miR-409-3p) were identified in adenovirus-infected children and provided a clear distinction between infected and healthy individuals. Potential host target genes were predicated and validated by qRT-PCR to study the impact of microRNAs on the host genes. Most of the target genes were involved in the MAPK signaling pathway and innate immune response. These highly upregulated microRNAs may have crucial roles in Adv pathogenesis and are potential biomarkers for adenovirus-infected pneumonia.

关键字 Human adenovirus，pneumonia， children，MicroRNA

分类：23. Pulmonology 呼吸
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Decreased Treg-derived miR-181a and miR-155 correlated with reduced number and function of Treg cells in allergic rhinitis children

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Background Regulatory cells (Tregs) have been proved to be deeply involved in allergic airway inflammation. This study aims to evaluate the expression of miRNA in children with AR and their association with Tregs as well as the severity of AR.
Methods Twenty-five AR children and 20 healthy children were enrolled in this study. The Treg-cell percentage and expression of IL-10 and TGF-β were detected by flow cytometry and enzyme-linked immunosorbent assay. The microRNA microarray analysis in purified Tregs was performed and differentially expressed microRNAs were confirmed by quantitative polymerase chain reaction (qPCR).
Results Children with AR had lower percentage of Tregs and expression of IL-10 and TGF-beta compared with control children. We found that significantly lower levels of miR-155 and miR-181a in Tregs from AR than healthy controls. Furthermore, intracellular miR-155 and miR-181a level were positively correlated with percentage of Tregs and expression of IL-10 and TGF-beta. Similarly, total nasal severity scores (TNSS) were found to be negatively correlated with miR-155 and miR-181a levels.
Conclusion Decreased Treg-derived miR-181a and miR-155 were correlated with reduced number and function of Tregs in AR children. The intracellular miR-155 and miR-181a levels may serve as predictors of disease severity in childhood AR.

关键字 Allergic rhinitis; Children; Regulatory T cells; miR-181a; miR-155

分类：23. Pulmonology 呼吸
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Distribution and expression of IL-17 and related cytokines in children with Mycoplasma pneumoniae pneumonia

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The pathogenesis of Mycoplasma pneumoniae pneumonia (MPP), especially the local immune responses of the lungs, is poorly understood. In this study, we used FCM (Flow Cytometry) to analyze IL-17 and related cytokines in plasma and bronchoalveolar lavage fluid (BALF) samples from 18 patients with general MPP (GMPP) and 30 patients with refractory MPP (RMPP). The levels of IL-1Ra, IL-6, IL-8, IL-17 and TNF-α were significantly elevated in the BALF of MPP children compared with the plasma ($P<0.01$). The plasma IL-6 levels in the children with RMPP were higher than those in the children with GMPP ($P<0.05$), but the IL-17 levels showed the opposite trend ($P<0.05$). The children with RMPP had significantly higher BALF levels of IL-8, IL-17 and TNF-α than the children with GMPP ($P<0.05$), and the elevated levels of IL-17 correlated with the focal size of the lung lesions ($P<0.05$). The elevated levels of IL-17 and related cytokines in the BALF could suggest that the local inflammatory response should be distinguished from the systemic inflammatory response in children with MPP. RMPP might involve aggravated inflammatory progression at the site of infection. The level of IL-17 might correlate with the extent and severity of the lung lesions in MPP.

关键字 Mycoplasma pneumoniae, cytokine, children, bronchoalveolar lavage fluid, interleukin-17

分类：23. Pulmonology 呼吸
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Identification of a novel compound targeting the nuclear export of influenza A virus nucleoprotein

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Although antiviral drugs are available for the treatment of influenza infection, it is an urgent requirement to develop new antiviral drugs regarding the emergence of drug-resistant viruses. The nucleoprotein (NP) is conserved among all influenza A viruses (IAVs) and has no cellular equivalent. Therefore, NP is an ideal target for the development of new IAV inhibitors. In this study, we identified a novel anti-influenza compound, ZBMD-1, from a library of 20,000 compounds using cell-based influenza A infection assays. We found that ZBMD-1 inhibited the replication of H1N1 and H3N2 influenza A virus strains in vitro, with an IC50 ranging from 0.41–1.14 lM. Furthermore, ZBMD-1 inhibited the polymerase activity and specifically impaired the nuclear export of NP. Further investigation indicated that ZBMD-1 binds to the nuclear export signal 3 (NES3) domain and the dimer interface of the NP pocket. ZBMD-1 also protected mice that were challenged with lethal doses of A/PR/8/1934 (H1N1) virus, effectively relieving lung histopathology changes, as well as strongly inhibiting the expression of pro-inflammatory cytokines/chemokines, without inducing toxicity effects in mice. These results suggest that ZBMD-1 is a promising anti-influenza compound which can be further investigated as a useful strategy against IAVs in the future.

关键字 influenza A virus； compound ZBMD-1; nucleoprotein; nuclear export

分类：23. Pulmonology 呼吸
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The study on ablation of Cbl-b promoting the production of IFN in pDC followed by inhibition of RSV amplification in macrophage

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E3 ubiquitin ligase Cbl-b plays important roles in immune system, but no any study reports its function on virus infection. Here we demonstrated that deletion of Cbl-b can ameliorate lung pathology caused by RSV infection due to increased production of IFNα/β in plasmacytoid dendritic cells (pDCs). RSV mainly infected macrophages. Further study suggested that Cbl-b can interact with IRF3, which is a key transcription factor for IFN expression, and mediate its K27-linked poly-ubiquitination on its K87 site. Thus, Type I IFN produced by pDCs protects macrophage from Respiratory Syncytial Virus infection.

关键字 respiratory syncytial virus; Cbl-b; interferon; pDC

分类：23. Pulmonology 呼吸
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Clinical characteristics of 42 cases of Mycoplasma pneumoniae pneumonia with plastic bronchitis in children

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Objective: To analyze the clinical characteristics of children with Mycoplasma pneumoniae pneumonia (MPP) complicated with plastic bronchitis (PB) in order to improve the level of diagnosis and treatment of PB.
Methods: The basic data of 42 cases of MPP in children with plastic bronchitis diagnosed by bronchoscopy at the respiratory department of Shanghai Children's Hospital from January 2018 to December 2020 were retrospectively analyzed, and the clinical manifestations, laboratory examination, etiology, imaging, treatment methods and outcomes of the children were analyzed.
Results: Among the 42 cases of MPP combined with PB, 19 cases were male (45.2%), 23 cases were female (54.8%), and 30 cases were older than 5 years (71.4%). Most cases occurred during the autumn and winter. All the patients had fever and cough, with an average heat course of 9.6 days. The C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), serum lactate dehydrogenase (LDH) level, D-dimer level, fibrinogen (FIB) level, IgE level in serum and IL-8 and IL-1β level in alveolar lavage fluid (BALF) were increased. The mixed infection rate was up to 52.4%, most of which were mixed viruses, and most of which were adenoviruses. Eight cases were admitted to the intensive care unit, 6 cases required endotracheal intubation-assisted ventilation, 25 cases required anti-inflammatory therapy with glucocorticoids, and 11 cases were immunocaptured with gamma globulin. Forty-two children had undergone more than one bronchoscopy and alveolar lavage. They were all better and discharged from the hospital.
Conclusions: MPP in children aged older than 5 years shows acute high fever, cough, rapid respiration, elevated CRP, ESR, LDH, D-dimer, FIB, and IgE, and lung consolidation/atelectasis, which require vigilance for PB. Timely bronchoscopy for interventional treatment can achieve a good therapeutic effect.

关键字 Mycoplasma pneumoniae pneumonia, plastic bronchitis, children, clinical characteristics

分类：23. Pulmonology 呼吸
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Analysis of clinical characteristics and risk factors of severe adenovirus pneumonia in children

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Objective: To understand the clinical characteristics and risk factors of severe adenovirus pneumonia (ADVP) in children, raise awareness and provide a basis for clinical diagnosis and treatment.
Methods: Clinical data from hospitalized children with ADVP treated at the Department of Respiratory Diseases of our hospital between July 2014 and June 2019 were analyzed retrospectively. Eighty-six patients were diagnosed with severe pneumonia, and related risk factors were analyzed.
Results: In total, 211 patients were enrolled in the study. 167 (64.9%) children aged 1 to 5 years old, and the onset was in winter and spring for 126 (59.7%) children. All patients had cough, and 116 (92.8%) patients with mild cases and 82 (95.4%) patients with severe cases had varying degrees of fever. The duration of fever in the severe ADVP group and mild ADVP group was 7.3 d and 5.4 d, respectively. The average hospital stays were 9.8 d and 5.8 d, respectively. There was no significant difference in the levels of WBC and ESR between the two groups, but the levels of N%, CRP, PCT and LDH in children with severe ADVP were significantly higher than those in the mild ADVP group. The univariate analysis showed that there were significant differences between the severe ADVP group and the mild ADVP group in ≥7 days of fever and high IgE ($P<0.05$). There was no significant difference in sex, age, onset season, mycoplasma infection, bacterial infection between the two groups ($P>0.05$). The multivariate logistic analysis showed that ≥7 days of fever and high IgE were independent risk factors for severe ADVP ($P<0.05$).
Conclusions: Children with severe ADVP have protracted fever, a strong inflammatory response and immune function disturbance. Immunological and comprehensive therapy should be given as early as possible clinically to improve prognosis.

关键字 Adenovirus pneumonia, Children, Risk factors

Category: 23. Pulmonology 呼吸
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Clinical predictors of wheezing among children infected with 2 Mycoplasma pneumonia

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Abstract Content Mycoplasma pneumonia (MP) was not just a common pathogen of respiratory tract infections, but could trigger the exacerbation of asthmatic symptoms in children with or without asthma. This study aimed to identify possible risk factors associated with wheezing among children diagnosed with MP infection.

Methods A retrospective analysis of medical records of children aged 28 days to 18 years old who visited the Shanghai Children's Hospital between January 2019 and January 2020 was carried out, and all children were then classified into three groups: two wheezing groups (with or without MP infection) and a non-wheezing group with MP infection. Information including patient's demographics, clinical features, laboratory data, and radiography findings was extracted from the electronic medical record system. Chest radiographs were reviewed independently by two board-certified, blinded pediatric radiologists .

Results A total of 1,512 patients were included in our study, and 21.9% of them belonged to the wheezing group without MP infection. Among 1,181 patients with MP infection, 295 people (25.0%) suffered from wheezing, and males accounted for 61%. Through the multivariable logistic regression analyses, we found that six variables were positively associated with wheezing attacks in children with MP infection: male gender (likelihood ratio [LR] = 2.124, 95% confidence interval [CI]: 1.478–3.053), history of allergy (LR= 3.301, 95% CI: 2.206-4.941), history of wheezing (LR = 7.808, 95% CI: 5.276-11.557), autumn in reference to summer (LR = 2.414, 95% CI: 1.500-3.885), non-end-point infiltration in reference to consolidation or pleural effusion (LR = 1.982, 95% CI: 1.348-2.914), and infiltration scope (LR = 1.773, 95% CI: 1.293-2.432). However, the model showed that the probability of wheezing after MP infection decreased as age increased (LR = 0.257, 95% CI: 0.196-0.337). Moreover, the area under the curve (AUC) of the regression model was as high as 0.901 (0.847-0.955).

Conclusion The model integrated with factors including gender, age, season, radiological patterns, infiltration scope, and history of allergy performed well in predicting wheezing attack after MP infection in children.

Key words mycoplasma pneumonia, wheezing, infiltration

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分类：23. Pulmonology 呼吸
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Comparison of Chinese and International version Evaluations of the Test for Respiratory and Asthma Control in Kids（TRACK）

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Background　Through the treatment and monitoring of wheezing children under 5 years of age who are positive for Modified Asthma Predictive Index (mAPI), follow-up assessment of the level of asthma control in children, and explore the Test for Respiratory and Asthma Control (TRACK)) The differences and feasibility between the Chinese version and the international version, and the Global Initiative for Asthma (GINA) in different nebulization intervention programs. Further explore the application value of the Chinese version of TRACK in the management of recurrent wheezing in children under 5 years of age.Method　The subjects of the study were wheezing cases diagnosed in the First Affiliated Hospital of Nanchang University from March 2018 to March 2020, and the age of 12 months to 59 months was met and mAPI was positive. A total of 240 children were included as follow-up subjects. Randomly divided into 2 groups, each with 120 cases, the intermittent high-dose atomized inhalation of budesonide suspension (BUD) group (intermittent high-dose group) completed 115 cases, the daily atomized inhalation BUD group (daily group)) 111 cases were completed. Follow-up treatment was followed up for 52 weeks. Every 4 weeks, a trained person evaluated the control level according to the GINA standard asthma control level, and completed the TRACK Chinese version and the international version of the scoring questionnaire. Taking the GINA standard control level classification as the "gold standard", through receiver operating characteristic curve (ROC curve) analysis, the best cut-off value for the control classification of wheezing children under 5 years of age who are mAPI-positive in the Chinese version of TRACK and the international version of the questionnaire was screened. And compare the consistency of the two evaluation methods.Results　In the intermittent high-dose group, the score control rate of the TRACK Chinese version from 4 to 52 weeks was lower than that of the international version, and the difference was significant (P<0.05). The agreement between the two was 75.1%, and the Kappa was 0.426. In the daily group, the score control rate of the Chinese version of TRACK in 4 and 8 weeks was lower than that of the international version, and the difference was significant (P<0.05). There was no significant difference in the score control rate between the Chinese version of TRACK and the international version from 12 to 52 weeks (P＞0.05), the agreement between the two is 93.2%, and the Kappa is 0.777. The area under the ROC curve of the TRACK international version and the Chinese version for diagnosis of asthma control are 0.904 and 0.887, respectively. The best cut-off values are 80 points and 75 points, respectively. The sensitivity is 74.9% and 75.3%, and the specificity is 84.8% and 80.5%.Conclusions　Both the Chinese version and the international version of TRACK can be used as an effective evaluation tool in the management of mAPI-positive wheezing children under 5 years old. The Chinese version of TRACK has stricter control levels than the international version. The clinical application should be combined with the intervention methods used by wheezing children. Comprehensive assessment, and at the same time, we should be alert to the potential risks of using high-dose inhaled corticosteroids.

关键字 Test for Respiratory and Asthma Control; Asthma management; Assessment; preschoolers

Category: 23. Pulmonology 呼吸
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Evolution of Forced Expiratory Indices in Asthmatic Children

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Abstract Content Asthma is the most common chronic respiratory disease in children, and these patients had repeated episodes of cough, breathing difficulty and wheeze. Their spirometric assessment is characterized by reversible airflow limitation and bronchial hyperresponsiveness. Regarding lung functions in children, it is known that different spirometric indices increase from childhood to young adulthood. These changes will then be followed by lung function decline as an aging process. Some studies suggested that patterns of lung function growth are useful predictor for childhood asthma outcomes. Nonetheless, there is limited data on the longitudinal changes of forced expiratory indices as measured by spirometry in children with asthma. This prospective study characterized changes in spirometric parameters and identified their determinants in asthmatic children.

Methods 181 Chinese children aged 5-15 years with physician-diagnosed asthma was recruited from pediatric clinics of our university-affiliated teaching hospital for annual follow-up for >=5 years and until adulthood when they were 18-25 years of age. Their demographics, family history, personal medical history and details of asthma status including disease control (as assessed by Asthma Control Test and Childhood Asthma Control Test), relevant prescriptions (including inhaled corticosteroid [ICS] and long-acting beta-agonists) and occurrence of asthma exacerbations were prospectively collected. They underwent pre-bronchodilator spirometry at baseline and then annually to measure forced expiratory indices. Generalized estimating equation (GEE) was used to analyze longitudinal changes in these spirometric parameters and their possible determining factors.

Results Patients' mean (standard deviation) age at baseline was 10.0 (2.7) years, and they were followed for an average of 12.5 years. Adjusting for covariates, we found significant decline in forced vital capacity (FVC) of 0.9%, but significant increase in ratio of forced expiratory volume in first second (FEV_1) to FVC (FEV_1/FVC) and forced expiratory flow at 25% to 75% of exhalation (FEF_{25-75}) of 1.3% and 2.8% per age respectively. Multivariate GEE revealed that children who outgrew asthma experienced 0.3% faster increase of FEV_1, 0.2% faster increase of FEV_1/FVC, and 0.6% faster increase of FEF_{25-75} per age. Compared with males, females had worse longitudinal lung function growth (increasing 0.3% less quickly in FEV_1 and FEF_{25-75}, and declining 0.3% more quickly in FVC per age). Patients with ICS treatment ever showed worse longitudinal lung function growth, manifested by increasing 0.3% less quickly in FEV_1/FVC and 0.4% less quickly in FEF_{25-75} per age. Age at baseline and body mass index showed significant disparity in longitudinal lung function change during childhood.

Conclusion This prospective study characterizes the evolution of different forced expiratory indices measured by pre-bronchodilator spirometry during childhood in Chinese children with asthma. A number of demographic and asthma-related factors influence long-term changes in these lung function parameters in our childhood population. (funded by Hong Kong Institute of Allergy Research Grant 2017)

Key words Asthma, child growth, forced expiratory index, lung function, spirometry

Reference Available upon request.

分类：23. Pulmonology 呼吸
679

Comparative analysis reveals significant peptides related to asthma mechanism

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Asthma is a kind of chronic inflammatory and allergic disease. Peptides play a significant rolein the immune response to asthma.Our study aims toidentify peptidomic profilesbetweenasthmatic mice and non-asthmatic mice.
Methods and Results:House dust mite (HDM) was utilized to build an asthmatic mouse model. Lung tissues weretested byhistological analysis and liquid chromatography-mass spectrometry (LC-MS/MS).Histological analysis of lung tissuesshowed eosinophils infiltration,thickening of the bronchial wall, swelling, and hyperemia of the mucosa.In which,108 of 1564peptides were identified as significant differentialexpression(fold change > 2 or fold change < 0.5, p-value< 0.05), containing 44 upregulated and 64 downregulated peptides. GO analysis demonstrated thatthe functional precursor proteins ofthe identified peptideswere primarily associated with actin polymerization or depolymerization, receptor-mediated endocytosis (RME), and regulation ofthe inflammatory response. KEGG analysis revealed the peptides were associated with SNARE interactions in vesicular transport, bacterial invasion of epithelial cells, and tight junction signalingpathways.Precursor proteins analysis revealed that peptides derived from glutamicacid-rich protein-like 3(SH3BGRL3) might be related to the incidence of asthma.
Conclusions: Our results put forward hypotheses on asthma and its mechanisms, and provide evidence for the candidate treatment sites of peptides in asthma.

关键字 Asthma, peptides, Liquid chromatography-mass spectrometry

分类：23. Pulmonology 呼吸
680

A study on the changes of the pathogenic spectrum of acute respiratory tract infection in children during COVID-19

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Objective To explore and analyze the changes of pathogen spectrum of acute respiratory tract infections(ARI) in children during Coronavirus disease 2019(COVID-19),in order to provide scientific evidence for their diagnosis and treatment.Methods Retrospectively compare and analyze the positive detection rate of viruses and atypical pathogens in children with ARI in different genders,different age brackets and each month as well as during the severe period of the epidemic and after the resumption of work and school in Jiangxi Children’s Hospital from January 1 to December 31 in 2020 with that in 2019.Results A total of 13584 virus and atypical pathogens were detected from January 1,2019 to December 31,2020,which meaned a positive rate of 34.36%.Among them,9647 cases were detected in 2019,3937 in 2020;8621 males,4963 females,male: female=1.74:1;8576 cases were 0~3 years old,3520 cases were 3~7 years old,1488 cases were 7~14 years old.The positive rate of pathogen detection in male and female children decreased in 2020 compared with 2019,the positive rate of pathogen detection was higher in female children.The positive rate of pathogen detection in all age groups was lower in 2020 compared with in 2019,and it was the highest at 7~14 years old.The positive rate of total pathogen detection in 2019 and 2020 was the highest in January.There were the top three of the pathogens which were detected positively from the ARI during COVID-19 that were MP,RSV,LP;MP,RSV,CP were in 2019;those were RSV,MP and LP during the severe epidemic from January to May in 2020;those were RSV,MP,LP in the same period in 2019;those were MP,RSV,LP from June to December in 2020 when people returned to work and to school,and MP,CP,LP in the same period in 2019.Conclusion During COVID-19,the positive rate of virus and atypical pathogens in children was lower than that in the same period in 2019;the pathogenic spectrum of virus and atypical pathogen in children with ARI has changed,MP,RSV,LP are the main pathogens in children with ARI during COVID-19.

关键字 Respiratory tract infections;Children;Pathogen;COVID-19

Category: 23. Pulmonology 呼吸
685

Effectiveness of Non-invasive Ventilation in Treating Infants aged 1 to 12 months with Severe Bronchiolitis: A Systematic Review and Meta-analysis

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Abstract Content This study was done to determine the effectiveness of noninvasive ventilation (NIV) in treating infants aged 1 to 12 months with severe bronchiolitis based on systematic review of literature and meta-analysis of quantitative results.
Methods We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for identification, screening and identification of eligible studies. Five databases (PubMed, Herdin, Cochrane Library, Google Scholar and Science Direct) were searched for relevant studies involving use of NIV among children with severe bronchiolitis. Included studies were assessed for quality and risk of bias.
Results There were 9 included eligible studies. The length of hospital stay and duration of respiratory support were significantly lower with the use of NIV compared with IMV (invasive mechanical ventilation) based on pooled standard mean difference (SMD) estimates; however, there was high statistical heterogeneity in the included studies. This can be attributed to differences in the mode of intervention used among studies, patient specific factors and viral virulence. Significant improvements in heart rate, oxygen saturation and tCO2 were seen in the included studies. One study showed statistically significant differences in changes in respiratory rate and improvement in respiratory status based on two bronchiolitis severity scores among infants placed on NIV[1].
Conclusion Fair to good-quality evidence from included studies revealed that there was significant reduction in length of hospital stay, duration of respiratory support, and improvements in respiratory parameters among infants who received NIV for severe bronchiolitis. Larger, well-designed clinical trials on the use of NIV among resource-limited settings wherein it may offer valuable clinical utility, are recommended for future study.

Key words non-invasive ventilation, bronchiolitis, infants, respiratory support, CPAP, BiPAP, NCPAP
Reference [1]Combret Y, Medrinal C, Prieur G, Le Roux. Non invasive ventilation improves respiratory distress in children with acute viral bronchiolitis. Minerva Anestesiologica. 2017 June 8. 83 (6) 624-37.

分类：23. Pulmonology 呼吸
772

Clinical characteristics and genetic analysis of interstitial lung disease in Chinese children

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Objective: Mutation in the surfactant protein C gene (SFTPC) is a cause of interstitial lung disease (ILD). Our objective was to investigate the clinical characteristics, outcome and influencing factors of ILD in Chinese children with SFTPC mutations.
Method: A total of 8 Chinese children with ILD heterozygous for SFTPC mutations that were treated in our hospital from January 2014 to December 2020 were included in our study. Candidate genes responsible for surfactant dysfunction were sequenced by next-generation sequencing. The clinical and genetic data were reviewed retrospectively.
Results: The children's onset age was before the age of 2 years, and one case was just after birth. The most significant clinical manifestations were cough, tachypnea, hypoxemia and failure to thrive. The most common mutation was p. Ile73Thr, which accounted for 87.5% (7/8) of our patients. Four patients whose onset was within 3 months, including 3 children with CMV infection, died.
Conclusion: p. Ile73Thr mutation of SFTPC was an important and common cause of ILD in the Chinese children. The clinical manifestations of ILD associated with this mutation are not specific. The severity and outcome of the disease may be affected by factors such as onset age and viral infection.

关键字 Clinical characteristic; Surfactant protein C gene; Interstitial lung disease; Mutation; Chinese

分类：23. Pulmonology 呼吸
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Study on the relationship between the level of serum 25-(OH) D 3 and the severity of community-acquired pneumonia in infants aged 1-36 months

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Objective: To observe the level of serum vitamin D (VD) in children with mild and severe community-acquired pneumonia (CAP), the incidence of VD deficiency in the two groups, the number of recurrent respiratory tract infection within 3 months after discharge and the number of re-hospitalization due to respiratory tract infection, so as to explore the relationship between VD and the severity of CAP, so as to provide a theoretical basis for VD level as the judgment of pneumonia condition and the risk prediction of recurrent respiratory tract infection.
Methods: A total of 230 CAP patients aged from 1 to 36 months in Shenzhen Children's Hospital from December 2019 to December 2020 were collected. According to the criteria for judging the severity of children's community-acquired pneumonia in 2013, the children were divided into severe pneumonia group (n = 81) and mild pneumonia group (n = 149cases). The level of serum VD in fasting vein was detected when the children were admitted to hospital, and the degree of serum VD deficiency in the two groups was calculated. Respiratory tract infection was followed up within 3 months after discharge.
Results: The serum VD level in the severe pneumonia group was lower than that in the mild pneumonia group (33.73 ±13.59ng/ml vs 37.59 ±13.20 ng/ml),t=2.096,P<0.05; and the serum VD deficiency rate in the severe pneumonia group was significantly higher than that in the mild pneumonia group (12.3% vs 4.7%), X2 =4.484，P<0.05.During the 3-month follow-up, the rate of recurrent respiratory tract infection in the severe pneumonia group was higher than that in the mild pneumonia group (34.6% vs 19.5%), X2 =5.284,P <0.05;and the rehospitalization rate due to respiratory tract infection in the severe pneumonia group was higher than that in the mild pneumonia group (9.9% vs 8.4%), but the difference was not statistically significant(X2 =1.647，P>0.05).
Conclusion：The level of serum VD is related to the severity of CAP. Detection of serum VD level plays an important role in the early evaluation of the disease and predicting the recurrence of respiratory tract infection, but the level of VD can not be used to predict the risk of re-hospitalization due to respiratory tract infection.

关键字 25-hydroxyvitamin D3; community-acquired pneumonia; severe pneumonia

分类：23. Pulmonology 呼吸
837

Childhood Tracheal Bronchus：A Case Report and Literature Review

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OBJECTIVE: To report a case of childhood tracheal bronchus and to improve the cognition, diagnosis and treatment of children with tracheal bronchus.
Methods: Retrospectively collect the clinical data of a child with tracheal bronchus and analyze the literature.
Results: The patient, a 9-year-old girl, was admitted to the hospital due to a dry cough with no obvious cause for more than 20 days. It was an irritating dry cough, which was obvious when inhaling deeply, occasionally waking up at night. The patient has no sputum, no nasal congestion and runny nose, etc. She was given "cephalosporin antibiotics, cetirizine, montelukast sodium" and nebulized "budesonide, terbutaline" and other drugs (the specific drugs and dosage are unknown) in the outside hospital, but no significant improvement was seen. Physical examination is generally acceptable. There is no history of wheezing. Laboratory test revealed total IgE: 67.5KIU/L, allergen-specific IgE: dog dander: (++++); chest CT showed: considering bronchial diverticulum, there is no obvious abnormality in the rest of the scan; otolaryngoscope: 1. Piriform fossa fistula is not excepted 2. Pharyngitis; neck ultrasound: cystic nodules in the thyroid (consider follicular cysts); thyroid function: no obvious abnormalities. Bronchoscopy showed: abnormal openings in the right main bronchus, consider repeating the right upper lobe; each bronchial mucosa is congested and edema, and a little flocculent secretion can be washed out during lavage. Combined with clinical manifestations, laboratory test and bronchoscopy, the diagnosis is: Tracheal bronchus (extra type). After 14 days of treatment such as nebulization, anti-infection, and immunomodulation, her symptoms improved and was discharged from the hospital. One week later, the outpatient follow-up did not complain of special discomfort.
Conclusion: Tracheal bronchus (TB) is a rare congenital airway dysplasia. It was first described by Sandifort as the right upper lobe bronchus originating from the trachea. According to the pathogenesis of TB, it can be divided into displaced type and extra type. The clinical manifestations are non-specific or diverse, which can cause repeated/continuous right upper lobe pneumonia, atelectasis, emphysema, repeated coughing, wheezing and other respiratory symptoms; or no clinical symptoms. Auxiliary examinations such as chest CT and airway three-dimensional reconstruction are often used to assist in diagnosis. In clinical practice, when the treatment effect of repeated or continuous coughing, wheezing, localized pneumonia and emphysema is not good, it is necessary to consider the tracheal bronchus. If possible, the fiberoptic bronchoscopy should be improved as soon as possible, which is conducive to the discovery of TB, airway stenosis and respiratory tract developmental abnormalities. The asymptomatic patients can be observed for a long time, conservative treatment; if there are repeated right upper lobe pneumonia, atelectasis, emphysema and poor drug treatment, bronchoalveolar lavage (BAL) can be given; if the symptoms are still not relieved, open the chest or thoracoscopic surgery to remove TB and related lung segments or lung lobes, and concurrent tracheoplasty.

关键字 childhood，tracheal bronchus

分类：23. Pulmonology 呼吸
1008

Application of multiplex PCR in etiological diagnosis of infant community acquired pneumonia

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【Abstract】
Background To explore the value of multiplex PCR in etiological diagnosis of infant community acquired pneumonia (CAP).
Methods The etiological results of hospitalized children aged 3-36 months with CAP from September to December 2019 in Shenzhen Children's Hospital were retrospectively analyzed. 192 children, who used multiplex PCR to detect influenza virus A (FluA), influenza virus H1N1 (FluA-H1N1), influenza virus H3N2 (FluA-H3N2), influenza virus B (FluB), respiratory syncytial virus (RSV), adenovirus (ADV), parainfluenza virus (PIV), human metapneumovirus (HMPV), human coronavirus (HCoV), human rhinovirus (HRV), human bocavirus (HBoV), mycoplasma pneumoniae (Mp) and chlamydia (Ch), were selected as multiplex PCR group. In addition, according to age, admission time, disease course at sampling and disease type and severity, those who used direct immunofluorescence to detect FluA, FluB, RSV, ADV, PIV and used fluorescence semi-quantitative PCR to detect MP, were matched 1:1 with multiplex PCR group as conventional test group. Two groups were compared and SPSS 22.0 was used for statistical analysis.
Result The total detection rate of multiplex PCR group was 81.25%, which was significantly higher than conventional test group (36.98%). Compared with the detection results of common pathogens in two groups, the detection rate of multiple PCR group was significantly increased (56.77% vs. 36.98%, $P<0.001$) and the increased detection rate of ADV and RSV was statistically significant ($P<0.05$). Using multiple PCR to detect pathogens, it found that RSV mainly existed in <12-month group, while MP mainly existed in 12-36-month group and showed that RSV and HRV are more common in wheezing children. 45 cases (23.44%) were infected with two or more than two pathogens. The most common pathogen of mixed infection was HRV and the mixed infection of HRV and MP was the most common type.
Conclusion With high sensitivity and ability to detect more pathogens, multiplex PCR can objectively reflect the etiological distribution and mixed infection of infants with CAP, which is helpful to clinical diagnosis and treatment.

关键字 infant; community acquired pneumonia; pathogen; multiplex PCR; direct immunofluorescence; fluorescence semi-quantitative PCR

分类：23. Pulmonology 呼吸
1014

Effect of nasal high flow oxygen therapy combined with respiratory function training in children with respiratory insufficiency

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Abstract:
Objective To investigate the clinical effect of nasal high-flow oxygen therapy combined with respiratory function training in children with respiratory insufficiency.
Methods forty hospitalized children with respiratory insufficiency aged 6-10 years were randomly divided into control group according to odd and even numbers. The children with respiratory insufficiency were given nasal heating and humidification high-flow oxygen therapy and symptomatic and routine nursing (n=20). Observation group: On the basis of nasal heating and humidification with high flow oxygen therapy, children's respiratory specialist nurses received vibration expectoration, effective cough, abdominal breathing, lip constriction breathing, and anti-resistance breathing function training, 3 times a day, 15 minutes each time (n=20).
Results Arterial blood gas analysis, respiratory work, activity endurance and lung function were measured before and after high-flow oxygen therapy combined with breathing training. FEV1 (1.34 VS 1.58), FVC (1.89 VS 2.09), FEV1/FVC and PEF observation group were better than the control group.
Conclusion through nasal high flow oxygen therapy in combination with respiratory function training can make children with respiratory insufficiency to reduce the incidence of complications such as respiratory failure, increasing well contraction ability and efficiency, reduce airway resistance and improve the tidal volume, improve the alveolar ventilation, reduce the power consumption of the breathing, breathing difficulties, ease of oxygen and carbon dioxide retention get improved, effectively improve lung compliance, Worthy of clinical promotion.

关键字 Key words: nasal heating and humidification high flow oxygen therapy; Children; Respiratory function training; Vibration expectoration drainage

分类：23. Pulmonology 呼吸
1026

Impact of hybrid onlinein-person asthma nursing care clinical regimen on the adherence to self-management of bronchial asthma in children

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Objective: To explore the impact of a hybrid online/in-person asthma nursing care clinical regimen on the adherence to at-home self-management of bronchial asthma in children.
Methods: This study selected a total of 100 children who attended the asthma clinic and asthma nursing care clinic at the Department of Respiratory Disease, Shenzhen Children's Hospital (Guangdong Province, China) from May 2019 to November 2019, including 50 children who attended the asthma clinic as the control group and 50 children who attended both the asthma and asthma nursing care clinics as the observation group. The control group was given routine asthma care and telephone follow-up. Asthma clinic physicians recommended the asthma nursing care clinic to the patients whom we later placed in the observation group. There, they were given at least 20 minutes of nursing intervention by specialized nurses during their first visit. During the nursing intervention, the online aspect of the treatment included (1) completing their personal profile on the online Guangdong Asthma Management platform, establishing standardized personal records, entering examination results, routine medications, and temporary backup drugs, and generating a personal asthma action plan (AAP); (2) downloading a mobile app for asthma management developed by Rongchang Zhilian Medical Science and Technology, with which they received assistance from the nurses in registering personal information and learning the various functions of the mobile app; (3) learning from nurses how to compose an electronic asthma diary using the patient's daily peak expiratory flow value, to check the AAP and how to conduct self-management and monitoring in accordance with the standards recommended by the AAP. Nurses also conducted health education. They assisted parents in finding and avoiding each patient's specific allergens. They taught proper techniques for using metered-dose nebulizers, inhalers, and peak flow meters and assessed the patients' use of these techniques. They assisted parents in making appointments for subsequent visits to ensure a timely follow-up. The rate of awareness of allergen avoidance, rate of accuracy of the administration of metered-dose nebulizers and inhalers, accuracy rate of peak flow meter use, and regular follow-up visits made by patients in both groups were compared after 6 months.
Results: After 6 months of intervention, all indicators were significantly better in the observation group than in the control group ($P < 0.01$). The proportion of patients who were aware of key allergens to avoid (97%), accuracy of metered-dose nebulizer and inhaler use (97%), accuracy of peak flow meter use (96%), rate of regular follow-up visits (95%) were significantly higher in the observation group than in the control group ($P < 0.01$; 42%, 62%, 42%, and 52%, respectively).
Conclusion: Through the development of a hybrid online/in-person asthma nursing care clinical regimen, these patients were able to establish personal records, and these records were traceable; through personalized health education, parents of the asthmatic children were able to cooperate more effectively with physicians in executing family treatment and self-monitoring of the disease. It also improved adherence to self-management in children and played the role of nursing care in the process of the disease recovery.

关键字 Keywords: Bronchial asthma; children; asthma care management; internet

分类：23. Pulmonology 呼吸
1062

A systematic review and meta-analysis of correlation between cough variant asthma and mycoplasma pneumonia in children

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Introduction: The present study was to explore the correlation between cough variant asthma (CVA) and repeated episodes of mycoplasma pneumonia in children.
Materials and Methods: Multiple databases were searched for relevant studies, and the articles that eventually satisfied the inclusion criteria were included. All the meta-analyses were conducted with the Review Manager 5.2. To estimate the quality of each article, the risk of bias table was performed. Totally 1223 patients with CVA and 1437 patients with simple cough (SC) were included.
Results: Finally, 9 studies including 2660 patients were included, who eventually satisfied the eligibility criteria. The results of heterogeneity test suggested that the serum level of IgE (MD = 80.69, 95%CI [77.75, 83.62], P < 0.001; P for heterogeneity <0.001, I2 = 95%), eosinophil count (MD= 2.93, 95%CI [2.72, 3.13], P < 0.001; P for heterogeneity < 0.001, I2 = 71%) and the number of children with positive IgM (OR = 4.44, 95%CI [3.73, 5.29], P < 0.001; P for heterogeneity = 0.63, I2 = 0%) were significantly different. The value of IgE in CVA was higher than that in SC, eosinophil count in CVA was higher than that in SC and the number of IgM positive children in the CVA group was higher than that in the SC group.
Conclusion: This study demonstrated a correlation between cough variant asthma and mycoplasma pneumonia.

关键字 Key words cough variant asthma, mycoplasma pneumonia, children.

分类：23. Pulmonology 呼吸
1087

Long noncoding RNA PTTG3P promotes the development of childhood asthma by targeting the miR-192-3p/CCNB1 axis

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Background: Increasing studies have suggested that long non-coding RNAs (lncRNAs) affect the regulation of immune responses, airway inflammation, and other pathological processes of asthma. In this study, we investigated the functions of the lncRNA PTTG3P in the progression of childhood asthma.
Methods: A competitive endogenous RNA network PTTG3P/miR-192-3p/CCNB1 was identified via bioinformatics analyses. Real-time qPCR and western blot were used to quantify gene and protein expression levels, respectively. Cell counting kit- 8 and transwell assays were used to evaluate the proliferation and migration abilities of bronchial epithelial cells (16HBE). Double luciferase reporter gene assay was used to validate the predictive targets in PTTG3P, miR-192-3p, and CCNB1.
Results: PTTG3P was highly expressed in the peripheral blood of children with asthma. Knocking down PTTG3P could inhibit the epithelial-mesenchymal transition (EMT), proliferation, and migration of 16HBE cells. Mechanistically, PTTG3P promoted childhood asthma progression by targeting the miR-192-3p/CCNB1 axis.
Conclusions: Childhood asthma development can be stemmed by targeting the PTTG3P/miR-192-3p/CCNB1 axis. This study provides potential diagnosis and treatment biomarkers for childhood asthma.

关键字 childhood asthma, epithelial mesenchymal transformation, long non-coding RNA, PTTG3P, miR-192-3p, ceRNA

分类：23. Pulmonology 呼吸
1088

Identification of Type 2-pediatric asthma based on single-cell transcriptomic analysis

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Type 2-pediatric asthma characterized by T2 cytokine-driven airway inflammation is the most common type of asthma. Recently, T2 cytokine inhibitors have reduced the exacerbation rates of asthma, but their ability to improve lung function is limited. Screening novel therapeutic strategies for Type 2-pediatric asthma patients is imperative. We obtained single-cell RNA sequencing (scRNA-seq) describing the chronic stimulation GSE145013 dataset with IL-13. Consensus clustering was performed to classify pediatric asthmatic patients from validation datasets GSE65204 and GSE40888, based on the cell marker genes. We found three cellular subtypes including ciliated cells, secretory cell 1, and secretory cell 2. The expression of CCL26, PRB1, and SLC9B2 was higher in secretory cell 1, while SCGB3A1 and BPIFA1 were higher in secretory cell 2. Consensus clustering based on the five cell marker genes produced two patient subtypes (C1 and C2). The expression of SCGB3A1 and BPIFA1 was higher in C2 subtypes, while CCL26, PRB1, and SLC9B2 was higher in C1 subtypes. Patients in C2 subtypes may more secretory cell 2, while the patients in C1 may have higher secretory cell 1 in the infiltrate. More Type 2 T helper cells were in the infiltrate in the C2 subtype, while type 1 T helper cells were higher in the C1 subtype. T2 cytokines (IL-13, IL-33, IL-3, IL-4, and TSLP) were expressed more in the C2 subtype, corresponding to Type 2-pediatric asthma. This study identified five cell marker genes to screen Type 2-pediatric asthma that could potentially be therapeutic targets for Type 2-pediatric asthma.

关键字 Type 2-pediatric asthma, single-cell sequence, transcriptomic analysis, immune cells, consensus clustering

分类：23. Pulmonology 呼吸
1109

Effectiveness of modified PIRO score in predicting prognosis of hospitalized children with CAP

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Background
Pneumonia is a major cause of mortality in children under five years old. The objective of this study was to evaluate whether a prognostic scale for estimation of incidence of severe pneumonia, risk of mechanically ventilation and mortality was applicable to children with community-acquired pneumonia (CAP).

Methods
Risk factors related to prognosis in children with CAP were identified by meta-analysis. Then a retrospective study was conducted in patients younger than 18 years with CAP admitted to either the respiratory department or intensive care unit from 2019 to 2020. The modified PIRO score consisted of several elements including predisposition (age<6 months, comorbidity), insult [SpO_2< 90%, delayed capillary filling time (>3s) and elevated procalcitonin (PCT) value (>0.5ng/ml)], response (multilobar or complicated pneumonia) and organ dysfunction (kidney dysfunction, liver dysfunction and respiratory failure). Patients were assessed by modified PIRO score and pediatric critical illness score (PCIS).

Results
Variables included in modified PIRO score were judged as risk factors of prognosis by meta-analysis. 4421 children with CAP were included in this study. With the increase of modified PIRO score, risk of ventilation support and mortality and the incidence of severe pneumonia increased in patients with CAP, respectively (P<0.05). While no significant association was found between mentioned prognosis above and groups stratified by PCIS (P>0.05).

Conclusion
Modified PIRO score is feasible for stratification of severity and prediction of adverse outcomes in children with CAP. Therefore, it is a prognostic tool to identify patients who are at high risk with severe pneumonia or poor prognosis at early stage.

关键字 modified PIRO score, CAP, prognosis

分类：23. Pulmonology 呼吸
1299

Analysis of Risk Factors of RMPP/SMPP in Children

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Objectives： We performed a clinical retrospective analysis of mycoplasma pneumoniae pneumonia (MPP) on hospitalized children, to screen out risk factors of refractory and severe mycoplasma pneumoniae pneumonia (RMPP/SMPP).
Methods: A retrospective analysis was performed on 1368 hospitalized children diagnosed with community acquired pneumonia (CAP) in the Department of Pediatrics of Xinhua Hospital from January 2019 to December 2019. The clinical manifestation and laboratory examination of 853 cases of MPP were analyzed to investigate risk factors of RMPP/SMPP.
Results： (1) The overall positive rate of mycoplasma pneumoniae (MP) was 62.4% (853 cases) in 1368 children with CAP. (2) Among 853 MP infection children, female 453 cases (66.7%), male 400 cases(58.1%), the positive rate of female was higher than that of male (P<0.05). Autumn(73.8%) is higher than summer(68.8%), spring(55.8%) and winter(53.7%) (P<0.05). The morbidity of MP infection in infant group, young children group, preschool group, school-age group were 20 cases(18.0%), 139 cases(50.4%), 276 cases(62.9%) and 418 cases(77.1%), respectively, and increased with age (P < 0.05) but tended to be younger.
(3) Among 41 viral infection children, female 12 cases (1.8%), male 29 cases(4.2%), the positive rate of male was higher than that of female (P< 0.05). Winter(5.6%) is higher than spring(4.0%), autumn(0.9%) and summer(0.7%) (P < 0.05). The morbidity of viral infection in infant group, young children group, preschool group, school-age group were 8 cases(7.2%), 19 cases(6.9%), 9 cases(2.1%) and 5 cases(0.9%), respectively, and decreased with age (P < 0.05). (4) Among the 221 co-infection children, the mixed infections of MP and virus were common. (5) The total days of fever, hospitalization days, lactate dehydrogenase (LDH), CD64 infection index, IL-6, IL-10 were independent risk factors for predicting RMPP (P < 0.05), and the cut-off points were 7.5 days, 5.5 days, 357 U/L, 0.2, 7.89 pg/mL and 11.35 pg/mL, respectively. (6) The total days of fever, hospitalization days, CRP, LDH, ferritin, CD64 infection index, IL-2R, IL-6, IL-10 were independent risk factors for predicting SMPP (P < 0.05), and the cut-off points were 7.5 days, 6.5 days, 15.5 mg/L, 358 U/L, 181 ug/L, 0.14, 997.50 U/mL, 7.89 pg/mL and 8.86 pg/mL, respectively.
Conclusions：(1) Mycoplasma pneumoniae was the dominant pathogen of CAP in children. 2019 may be a peak time of MP infection. The positive rate of female was higher than that of male, and autumn is higher than summer, spring and winter, increased with age but tended to be younger. (2) The total days of fever, hospitalization days, lactate dehydrogenase (LDH), CD64 infection index, IL-6, IL-10 were independent risk factors for predicting RMPP, and the cut-off points were 7.5 days, 5.5 days, 357 U/L, 0.2, 7.89 pg/mL and 11.35 pg/mL, respectively. (3) The total days of fever, hospitalization days, CRP, LDH, ferritin, CD64 infection index, IL-2R, IL-6, IL-10 were independent risk factors for predicting SMPP, and the cut-off points were 7.5 days, 6.5 days, 15.5 mg/L, 358 U/L, 181 ug/L, 0.14, 997.50 U/mL, 7.89 pg/mL and 8.86 pg/mL, respectively.

关键字 Children; Mycoplasma pneumoniae pneumonia; Cytokines; CRP; Lactate dehydrogenase; Ferritin

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1303

Clinical application of transbronchial cryotherapy in the diagnosis and treatment of tracheobronchial tuberculosis in children

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Objective: To explore the clinical utility of bronchoscopy and transbronchial cryotherapy in children with Tracheobronchial tuberculosis (TBTB).
Methods: Retrospective study was conducted to collect the clinical data of 10 hospitalized children who underwent bronchoscopy and were diagnosed as TBTB and in the Department of Pediatrics of Peking University First Hospital and the Department of Pediatric Respiratory Medicine of the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University from January 2011 to October 2019. The clinical characteristics of TBTB in children, and the efficacy and safety of bronchoscopy and transbronchial cryotherapy were summarized through descriptive analysis.
Results: The onset age of 10 children (6 males and 4 females) ranged from 1-14 years. The clinical manifestations included fever (8/10), cough (7/10) and hemoptysis (2/10). Purified protein derivative test and interferon-γ release assay were performed in 9 and 10 patients respectively, the results were all positive. Chest CT examination was performed in all patients, and 8 patients had hilar and/or mediastinal lymphadenopathy. All patients underwent pediatric bronchoscopy in time, in 9 patients bronchus was found to be blocked in varying degrees by granulation tissue and caseous necrosis and in the remaining patient, we noticed obvious congestion and edema in bronchial mucosa. The bronchoscopic manifestations included 8 cases of lymph node fistula type, 1 case of granulation proliferative type and 1 case of inflammatory infiltration type. Pathological biopsies were performed in 7 cases, the findings were consistent with the pathological characteristics of tuberculosis. Nine patients were treated by pediatric bronchoscopic intervention, with 8 transbronchial cryotherapy by flexible bronchoscopy, and among them, 2 patients were treated by simultaneous rigid bronchoscopy. After 1-3 times of transbronchial cryotherapy, the blocked bronchial lumina in 8 cases were all recanalized, and the curative effect was significant without any serious complications.
Conclusions: Bronchoscopy plays an important role in the diagnosis of TBTB in children and is helpful for its classification. Also, transbronchial cryotherapy has good efficacy and safety for TBTB in children, especially for the granuloproliferative type or lymph node fistula type.

关键字 Tuberculosis; Child; Bronchoscopy; Cryotherapy

分类：23. Pulmonology 呼吸
1305

Association of ABCB1 C3435T gene polymorphism with azithromycin concentration in children with mycoplasma pneumoniae pneumonia

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Objective To investigate the association between ABCB1 C3435T gene polymorphism with plasma azithromycin concentration and pulmonary epithelial lining fluid (ELF) azithromycin concentration of children with mycoplasma pneumoniae (MP) pneumonia. **Subject** Children with MP pneumonia who underwent BAL after intravenous injection of azithromycin for 7 days. **Methods** From July 2018 to December 2019, 100 hospitalized children diagnosed with MP pneumonia and required broncho alveolar lavage (BAL) in the Department of Respiratory of the Capital Institute of Pediatrics were enrolled, and they underwent BAL after intravenous injection of azithromycin for 7 days. On the day of BAL, peripheral blood samples and bronchoalveolar lavage fluid (BALF) samples were collected and clinical data were recorded. Azithromycin concentrations in plasma and BALF samples were determined by liquid chromatography-mass spectrometry (LC-MS/MS), urea concentrations in serum and BALF were determined by enzyme and fluorescence spectrophotometry, azithromycin concentrations in pulmonary epithelial lining fluid (ELF) were calculated by urea dilution method, and ABCB1 C3435T genotypes were detected by Sanger sequencing. Statistical analysis of clinical data, plasma azithromycin valley concentration, pulmonary ELF azithromycin concentration of children with different genotypes. **Results** Plasma azithromycin valley concentration: the results of each genotype group were similar, about 0.29 ±0.08 μ g / mL, and less than the lowest concentration that inhibits 90% MP growth (MIC90, 32μg/mL). Pulmonary ELF azithromycin concentration: CC genotype group (42.19 ±38.68 μ g / mL) was significantly higher than TC genotype group (19.81 ±13.67 μ g / mL) and TT genotype group (14.51 ±9.18 μ g / mL) ($P < 0.05$). The proportion of children's pulmonary ELF azithromycin concentration more than MIC90 of MP: the proportion of CC genotype group(64.3%) was significantly higher than that of TC genotype group (18.2%). **Conclusion** There was no correlation between ABCB1C3435T gene polymorphism and plasma azithromycin concentration, but ABCB1C3435T gene polymorphism was correlated with the pulmonary ELF azithromycin concentration. The pulmonary ELF azithromycin concentration of CC genotype was significantly higher than that of TC genotype and TT genotype.

关键字 Mycoplasma pneumoniae pneumonia; Azithromycin; ABCB1 C3435T polymorphism; Blood concentration; Lung epithelial lining fluid; Drug concentration; Children

分类：23. Pulmonology 呼吸
1312

Correlation between Course of Azthromycin and Drug Concentrations in Children with Mycoplasma pneumoniae Pneumonia

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Objective To investigate the correlation between the course of azithromycin and the drug concentration of blood or lung epithelial lining fluid (ELF) in children with Mycoplasma pneumonia (MP) pneumonia.

Methods From July 2018 to December 2019, 100 hospitalized children diagnosed with MP pneumonia and required broncho alveolar lavage (BAL) in the Department of Respiratory of the Capital Institute of Pediatrics were enrolled, and they were given intravenous azithromycin treatment. According to the course of intravenous azithromycin before BAL operation, they were divided into intravenous 4 days group (continuous intravenous administration for 4 days), intravenous 7 days group (continuous intravenous administration for 7 days), intravenous 10 days group (continuous intravenous administration for 10 days), 3 days interval group (continuous intravenous administration for 7 days and withdrawal for 3 days) and the second course of intravenous treatment for 4 days (continuous intravenous administration for 7 days and withdrawal for 3 days, then continue the second course of intravenous administration for 4 days). Peripheral blood and broncho alveolar lavage fluid (BALF) specimens were collected on the day of BAL operation. The concentration of azithromycin in the specimens was detected by liquid chromatography-mass spectrometry, and the pulmonary ELF drug concentration was calculated by the urea dilution method. Statistical analysis of clinical data, plasma azithromycin concentration and pulmonary ELF azithromycin concentration in children with different azithromycin treatment groups were performed by SPSS.

Results Plasma azithromycin concentration in intravenous 4-day group (0.24 ±0.1μg/mL), intravenous 7-day group (0.29 ±0.08μg/mL) and intravenous 10-day group (0.32 ±0.02μg/mL) was similar, and significantly higher than that in 3-day interval group (0.13 ±0.07μg/mL) ($P < 0.05$). Pulmonary ELF azithromycin concentration: intravenous 10-day group (43.17 ±32.21μg/mL) was significantly higher than intravenous 4-day group (21.76±21.01 μg/mL) and intravenous 7-day group (26.17 ±19.57μg/mL) ($P < 0.05$). The drug withdrawal interval group (28.10 ±13.68μg/mL) was similar to those before drug withdrawal (continuous vein for 7 days) , and the difference was not statistically significant ($P > 0.05$).Plasma azithromycin concentration of the five treatment groups was extremly lower than the lowest concentration that inhibits 90% MP growth (MIC90, 32μg/mL).The proportion of children's pulmonary ELF azithromycin concentration more than MIC90 of MP: the proportion of intravenous 10-day group was 80%, which was significantly higher than that of intravenous 4-day group (20%) and intravenous 7-day group (32.5) ($P < 0.05$).

Conclusion During the 4-10 days of first course after intravenous injection of azithromycin in children with MP pneumonia. The plasma azithromycin concentration was low and stable, which was always much lower than MIC90 of MP; The pulmonary ELF azithromycin concentration which was 93.61-141.84 times higher than that in plasma, increased with the prolongation of the course of treatment .The number of children whose pulmonary ELF azithromycin concentration can effectively inhibit MP, will be larger and larger with the prolongation of the course of treatment. After continuous

intravenous administration for 7 days and withdrawal for 3 days, the plasma azithromycin concentration about decreased by 50% , while the pulmonary ELF azithromycin concentration remained stable.

关键字 Mycoplasma pneumoniae pneumonia; Azithromycin; Course of Treatment; Blood concentration; Lung epithelial lining fluid; Drug concentration; Children

分类：23. Pulmonology 呼吸
1336

IL-13R130Q enhances asthma susceptibility by regulating the functional activity of airway smooth muscle cells

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Background: Interleukin (IL)-13, a Th2-type cytokine, plays a pivotal role in the pathogenesis of asthma through its direct effects on airway smooth muscles, which has been observed undergoing marked phenotypic modulation in asthma. We previous study has shown that, IL-13 R110Q, a naturally occurring IL-13 polymorphism, confers enhanced functional activity in cultured human bronchial smooth muscle cells. In the present study, we aimed to determine whether the IL-13 R110Q variant would effect the phenotype of human BSM. Methods: After treating with increasing concentration of IL-13R130Q or IL-13 for 24h, we performed real-time PCR to characterize the endogenous expression of il-5 and il-4 by HBSM. We tested the effect of IL-13R130Q and IL-13 on acetylcholine-induced changes in intracellular calcium concentration by the fluorescent probe Fluo-3/AM with flow-cytometric analysis; we investigated the proliferative activities by cell proliferation assay with CCK-8 kit; HBSM cell migration was analyzed by using Boyden chamber assay. Results: Our results show that IL-13 R130Q was significantly more active than IL-13 in inducing BSM migration, proliferation, increase contractile responses and secret il-5, il-4 in HBSM. Conclusions: Collectively, our data indicate that natural variation in the coding region of IL13 may contribute to asthma through hBSM phenotypic modulation in asthma.

关键字 IL-13R130Q; Bronchial smooth muscle cell; Functional activity; Asthma

分类：23. Pulmonology 呼吸
1377

Study of rhIFNα2b versus Lanqin oral liquid in treatment of herpangina in children

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ABSTRACT Background Herpangina is an acute upper respiratory tract infection caused by enterovirus infection in children.Clinical manifestations are mainly characterized by herpes of pharyngeal isthmus, salivation and fever, which will have adverse effects on the health of children. A number of studies have shown that recombinant human interferonα-2b (rhIFNα2b) spray can shorten the overall course of herpetic angina and is safe. There are also many reports showing that Lanqin oral liquid can significantly improve the efficacy of children with herpetic angina, effectively shorten the time of fever and herpes resolution, without increasing the occurrence of adverse reactions. The efficacy of different drugs has always been the focus of clinical discussion. The objective of this study was to compare the efficacy and safety of rhIFα2b aerosol oropharyngeal spray, Lanqin oral liquid and their combination in the treatment of herpetic angina in children.
Objective To observe the therapeutic effect of rhIFNα2b spray and Lanqin oral liquid on children with herpetic angina.
Methods 90 children diagnosed with herpetic angina were randomly divided into rhIFNα2b spray treatment group (interferon group) and Lanqin oral liquid treatment group (Lanqin group) and two-drug combination treatment group (combined group) according to the order of treatment, 30 cases in each group, and the therapeutic effect of the three groups was observed.All the children were given antipyretic drinking water and other symptomatic support on the basis of treatment.Interferon group was treated with rhIFNα2b spray.Lanqin group was given Lanqin oral liquid,4 days of treatment.The combined treatment group was simultaneously treated with rhIFNα2b spray and Lanqin oral liquid.Those who recover early are no longer given medication.Efficacious: after treatment, the child's temperature returned to normal within 48 hours, clinical symptoms were significantly improved, appetite was significantly improved, pharyngeal ulcer was significantly improved, herpes disappeared.Effective: after treatment, within 72 hours, the child's temperature returned to normal, clinical symptoms improved, appetite significantly improved, pharyngeal ulcer improved, herpes improved.Ineffective: After 72 hours of treatment, the clinical symptoms of the child still did not improve or worsen.
Results In interferon group, there were 21 males and 9 females,average age of 3.3±1.6 years, with an average course of disease of 1.1±0.5 days. Lanqin group: 18 males and 12 females,average age of 3.3±1.2 years, with an average course of disease of 1.3±0.9 days. Combined group: 18 males and 12 females, average age of 3.7±1.4 years, with an average course of disease of 1.0±0.5 days.There was no significant difference in age, gender, disease course and other general information among the three groups (P>0.05).Lanqin group: the total effective rate was 83.3%; rhIFNα2b group the total effective rate was 80%. In the combined treatment group, the total effective rate was 93.3%. There was no statistical significance in total effective rate among the three groups (P>0.05).And there was no statistically significant difference between Lanqin group and rhIFNα2b group (P>0.05). However, the combination treatment of Lanqin group and rhIFNα2b group could

significantly shorten the time of herpes subside fever (P<0.05).No obvious adverse reactions were observed in the three groups (P>0.05).
Conclusions Lanqin oral liquid and rhIFNα2b spray have similar clinical efficacy in the treatment of herpetic angina. The combination of the two drugs can not improve the clinical efficacy, but can accelerate the disappearance of clinical symptoms and signs and shorten the overall course of disease with good safety. Personalized treatment can be carried out according to the specific situation of children.
关键字 Key words:Herpangina;Lanqin oral liquid;rhIFNα2b.

分类：23. Pulmonology 呼吸
1380

Identifying Key Genes and Functionally Enriched Pathways in Th2-high asthma by Weighted Gene Co-Expression Network Analysis

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Purpose: Asthma is a chronic lung disease characterized by reversible inflammation of the airways. The imbalance of Th1/Th2 plays a significant role in the mechanisms of asthma. The aim of this study was to identify Th2-high subgroup of asthma related key genes and functionally enriched pathways using the weighted gene co-expression network analysis (WGCNA). Materials and Methods: The gene expression profiles of GSE4302, including 42 asthma patients and 28 controls, were selected from the Gene Expression Omnibus (GEO). Gene network was constructed and genes were classified into different modules using WGCNA. Gene ontology (GO) was performed for further exploring the potential function of the genes in the most related module. In addition, the expression profile and diagnostic capacity (ROC curve) of interested hub genes were verified by dataset GSE67472.Results: In dataset GSE4302, asthma subjects were divided into Th2-high and Th2-low groups according to the expression of genes SERPINB2, POSTN and CLCA1.WGCNA was constructed and genes were classified into 7 modules. Among them, the red module was most closely associated with Th2-high asthma, which contained 60 genes. These genes were significantly enriched in different biological processes and molecular functions. A total of 8 hub genes (TPSB2, CPA3, ITLN1, CST1, SERPINB10, CEACAM5, CHD26 and P2RY14) were identified and these genes (except TPSB2) expression levels were confirmed in dataset GSE67472. ROC curve validated that these 8 genes' expression levels exhibited excellent diagnostic efficiency for Th2-high asthma and Th2-low asthma.Conclusion: The study applied WGCNA to provide a novel perspective of Th2-high asthma, and the hub genes and potential pathways involved may beneficial for the diagnosis and managements of Th2-high asthma.
Keywords: asthma, weighted gene co-expression network analysis (WGCNA), hub gene, gene ontology
关键字 asthma, weighted gene co-expression network analysis (WGCNA), hub gene, gene ontology

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1386

Title: Clinical features of pneumomediastinum in children: 44 case reports

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Abstract Content Pediatric pneumomediastinum is a condition rarely observed in children. This study evaluated the clinical characteristics of pediatric patients with pneumomediastinum seen over a period of 12 years.

Methods This retrospective study looked at patients aged between 0 - 16 years who were diagnosed with pneumomediastinum on medical records between January 2009 and June 2021 in an emergency room at Children's Medical Center, Kitakyushu City YAHATA Hospital, Japan. The data was obtained by conducting a search of the medical records between the dates mentioned, using the search term "pneumomediastinum" and confirming the diagnosis by correlating radiological findings with the diagnosis given. Cases of suspected pneumomediastinum which were not confirmed by radiological investigations were excluded from the study.

Results Forty-four cases were identified (31 male, 13 female). The median age of patients was 12 years (range,1-16 years). 31 (70.4%) cases were hospitalized. The median length of stay was 6 days. Chest pain (70.4%), neck pain (52.2%), and odynophagia (18.2%) were the most common reported symptoms. The most common causes of onset were shouting while playing sports (54.5%), unknown cause (20.4%), and acute asthma attacks (6.8%).
Although the mainstay of treatment for pneumomediastinum is conservative management, 10 cases (22.7%) were prescribed antibiotics. 8 of these were prescribed as prophylaxis against mediastinitis or other infections resulting from pneumomediastinum.
Over the whole 12-year period, we observed a decreasing trend in the overall number of antibiotic prescriptions. Looking at the data in 3-year periods: 2009 - 2011, n = 5 of 9 (55.6%); 2012 - 2014, n = 2 of 2 (100.0%); 2015 - 2018, n = 2 of 14 (14.3%); 2018 - 2021, n = 1 of 20 (5.0%).
Of 6 cases requiring oxygen therapy, only one patient was a case of spontaneous pneumomediastinum; 4 were pneumomediastinum secondary to acute respiratory conditions (asthma exacerbation, pneumonia) ,and one patient of pneumomediastinum was caused by an ingested foreign body.
No cases led to complications of pneumothorax or mediastinitis.
All of the cases used either plain chest radiographs or a computed tomography (CT) scan for diagnosis. Radiographs and CT scans were often used repeatedly in follow-up. Ultrasound imaging was used to support diagnosis in follow-up in 6 cases and of those, pneumomediastinum was detected in 5 cases, with one patient only detectable by chest radiograph.

Conclusion Previous studies have indicated that pediatric pneumomediastinum primarily affects males and the results of our study also support this finding.
The current use of antibiotics for preventing secondary infection could be reconsidered as our study showed that the decreasing trend of using antibiotics as part of the management plan did not affect the numbers of infection.

Although our study suggests that it is rare to develop further complications of pneumomediastinum in children, it remains essential to consider pneumomediastinum in the list of differential diagnoses in those presenting with chest pain, neck pain, and odynophagia as the potential risk of complications is still present.
As there are concerns surrounding radiological exposure in children, the use of ultrasound imaging could potentially be an effective method of decreasing radiation exposure, while maintaining reasonable diagnostic rates. There is scope for further study of this modality in pediatric pneumomediastinum.

Key words Pneumomediastinum, chest radiograph, ultrasound
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分类：23. Pulmonology 呼吸
1542

Exosomes derived from human bone marrow-mesenchymal stem cells suppress proliferation of bronchial smooth muscle cells and lung injury in asthmatic mice through a microRNA-188/JARID2/Wnt/β-catenin axis

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Abstract
Objective: The functions of exosomes in allergic diseases have aroused increasing concerns. This paper aims to explore the effects of exosomes derived from human bone marrow-mesenchymal stem cells (hBM-MSCs) on the asthma progression and the mechanism involved.
Methods: Exosomes were extracted from hBM-MSCs and identified. Human bronchial smooth muscle cells (BSMCs) were induced with transforming growth factor (TGF)-β1 to mimic an asthma-like condition in vitro and then treated with exosomes. The proliferation, apoptosis and the migration potentials of BSMCs were detected. Differentially expressed microRNAs (miRNAs) in cells after exosome treatment were screened using a microarray analysis. The target mRNAs of miR-188 were explored. Altered expression of miR-188 and JARID2 was introduced into exosome-treated BSMCs. A mouse model with asthma was induced by ovalbumin (OVA) and treated with exosomes for in vivo study.
Results: The hBM-MSC-derived exosomes significantly reduced the abnormal proliferation and migration of the TGF-β1-treated BSMCs. miR-188 was the mostly enriched miRNA in exosomes, and JARID2 was identified as a mRNA target of miR-188. Either downregulation of miR-188 or upregulation of JARID2 blocked the protective effects of exosomes on BSMCs. JARID2 activated the Wnt/β-catenin signaling pathway. In the asthmatic mice, the hBM-MSC-derived exosomes reduced inflammatory cell infiltration, mucus production and collagen deposition in murine lung tissues.
Conclusion: This study suggested that hBM-MSC-derived exosomes suppress proliferation of BSMCs and lung injury in asthmatic mice through the miRNA-188/JARID2/Wnt/β-catenin axis. This study may provide novel insights into asthma management.
Keywords: Human bone marrow-mesenchymal stem cells; Exosomes; microRNA-188; JARID2; Wnt/β-catenin; Asthma; Bronchial smooth muscle cells

关键字 Exosomes，roliferation of bronchial smooth muscle cells and lung injury ，asthmatic mice

分类：23. Pulmonology 呼吸
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Association between Mycoplasma pneumoniae induced bronchiolitis in infant and wheezing: a 2 years follow-up

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Objective: To assess the association between Mycoplasma pneumoniae (MP) induced bronchiolitis in infant and wheezing; To explore the risk factors of wheezing after MP induced bronchiolitis.
Methods: 95 patients with MP induced bronchiolitis in pediatric respiratory ward of Shengjing Hospital from January 2016 to December 2018 were selected and followed-up for 2 years. The patients were divided into wheezing group (34 cases) and non-wheezing group (61 cases) . According to the wheezing time after MP induced bronchiolitis, the patients were also divided into Recurrent wheezing group(22 cases) and non-RW group(73 cases) .The clinical data of the selected cases were collected and the risk factors were analyzed.
Results: Low SaO2(＜92%) in hospitalization, Parental history of allergic rhinitis or eczema and Parental smoking were the risk factors of wheezing occurence after MP induced bronchiolitis (P < 0.05). Cases with Low SaO2(＜92%) in hospitalization had six -fold higher for wheezing occurence (OR:6.174, 95% confidence interval [CI]: 1.286-54.273; P < .05).Cases with Parental history of allergic rhinitis or eczema had four -fold higher for wheezing occurence (OR:4.061, 95% confidence interval [CI]: 1.239-13.311; P < .05).Cases with Parental smoking had three -fold higher for wheezing occurence (OR:3.374, 95% confidence interval [CI]: 1.076-10.573; P < .05).Positive response to allergens, Low SaO2(＜92%) in hospitalization, and Parental smoking were the risk factors of recurrent wheezing occurence after MP induced bronchiolitis (P < 0.05) .Cases with Positive response to allergens had seven -fold higher for recurrent wheezing occurence (OR:7.333, 95% confidence interval [CI]: 1.807-54.273; P < .01).Cases with Low SaO2(＜92%) had seven -fold higher for recurrent wheezing occurence (OR:7.279, 95% confidence interval [CI]: 2.012-26.723; P < .01).Cases with Parental smoking had five -fold higher for recurrent wheezing occurence (OR:5.314, 95% confidence interval [CI]: 1.525-18.516; P < .01).
Conclusion: The patients who had the risk factors of Low SaO2(＜92%) in hospitalization, Parental history of allergic rhinitis or eczema and Parental smoking should be attention to the wheezing occurence after MP induced bronchiolitis. Positive response to allergens, Low SaO2(＜92%) in hospitalization, and Parental smoking were the risk factors of recurrent wheezing occurence after MP induced bronchilitis.

关键字 bronchiolitis; wheezing; risk factors;Mycoplasma pneumoniae

分类：23. Pulmonology 呼吸
1562

Clinical observation on the treatment for RSV induced bronchiolitis by nebulized recombinant human interferon α 1b.

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Objective To evaluate the clinical effacy on tthe treatment for RSV induced bronchiolitis by nebulized recombinant human interferon α 1b. Methods The clinical data of patients admitted to the pediatric ward of the Sheng Jing Hospital for acute ronchiolitis terated with nebulized inhalation of recombinant human interferon α 1b were analyzed retrospectively. The clinical efficacy of nebulized inhalation of recombinant human interferon α 1b in the treatment of children with RSV induced bronchiolitis and non- RSV induced bronchiolitis were evluated by the scores of clinical symptoms and signs . Children infected by RSV were divided into early treatment group and late treatment group according to whether the onset of RSV infection was within 72 hours after the start of nebulized inhalation of recombinant human interferon α 1b. Results The improvement rates of the clinical symptoms and the signs of the children with RSVinduced bronhiolitis and non RSV induced bronhiolitis after Day 1,3 and 5 treatment with nebulized recombinant human interferon α 1b were analysed , there was no significant difference between the two groups (p > 0.05) . There were also no significant differences in the improvement rates of clinical symptoms, physical signs and the length of hospital stay between the early and late stage of RSV infected children treated with nebulized inhalation of recombinant human interferon-1b on Day 1,3 and 5.(p > 0.05). Conclusions The clinical efficacy of nebulized inhalation of recombinant human interferon α 1b was similar between the treatment of children with and without RSV infection and the early and late stage of RSV infected children

关键字 bronchiolitis； respiratory syncytial virus; human recombinant interferon α1b; inhalation

分类：23. Pulmonology 呼吸
1564

Characteristics of Medicine Use for Children with asthma in China: a Nationwide Population-based Study

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Objective: To analyze the use of anti-asthma drugs in Chinese children, based on the 2015 Medical Insurance Data in China.
Methods: A cross-sectional study design was employed to conduct a comprehensive analysis for their use of anti-asthmatic drugs in 2015.
Results: 308,550 children were treated under coverage of medical insurance, 2,468 were eligible for inclusion. Compared with the guidelines for the diagnosis and treatment of asthma in China and the current status of asthma care in European and American countries, the use rates of ICS and SABA in children with asthma in China are lower, but the use rates of OCS, LABA, and theophylline are higher, especially in the central and western regions.
Conclusion: This is the first comprehensive analysis of anti-asthma medication among children in China. Major efforts are still needed to strengthen the education and popularization of the GINA programs and China's guidelines for asthma diagnosis and treatment.

关键字 Key words：pediatrics, asthma, medication, medical insurance data, CHIRA database, ICS, SABA.

分类：23. Pulmonology 呼吸
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Primary alveolar soft-part sarcoma of the lung in children: a case report and literature review

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Alveolar soft-part sarcoma (ASPS) is a rare sarcoma of soft tissue characterized by ASPSCR1-TFE3 gene fusion. The ASPS involving the lung is mostly metastatic, while the primary ASPS involving the lung occurs more rarely. At present, there are only few cases affected by this condition, so no standard treatment or recommended first-line treatment has been proposed. To date, 10 cases of primary pulmonary ASPS have been reported, among which three were pediatric patients. Herein, we reported on another case of primary ASPS, which might be with the earliest onset reported thus far. This case was diagnosed through surgical pathology, immunohistochemistry, high-throughput sequencing, and PET-CT results. It is the only one treated with a new molecular targeted therapy with an antiangiogenic agent. In this report, surgery was used to excise the lesion as much as possible, and its combination with chemoradiotherapy and anti-angiogenic agent (anlotinib) may provide an important reference for the development of standard treatment or first-line treatment for these children patients. This case may provide an important reference for the development of standard treatment or first-line treatment for these children patients.

关键字 Alveolar soft-part sarcoma,anlotinib,ASPSCR1-TFE3,children

分类：23. Pulmonology 呼吸
1609

Significance of RNA N6-Methyladenosine Regulators in the Diagnosis and Subtype Classification of Childhood Asthma Using the Gene Expression Omnibus Database

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RNA N6-methyladenosine (m6A) regulators play important roles in a variety of biological functions. Nonetheless, the roles of m6A regulators in childhood asthma remain unknown. In this study, 11 significant m6A regulators were selected using difference analysis between non-asthmatic and asthmatic patients from the Gene Expression Omnibus GSE40888 dataset. The random forest model was used to screen five candidate m6A regulators (fragile X mental retardation 1, KIAA1429, Wilm's tumor 1-associated protein, YTH domain- containing 2, and zinc finger CCCH domain-containing protein 13) to predict the risk of childhood asthma. A nomogram model was established based on the five candidate m6A regulators. Decision curve analysis indicated that patients could benefit from the nomogram model. The consensus clustering method was performed to differentiate children with asthma into two m6A patterns (clusterA and clusterB) based on the selected significant m6A regulators. Principal component analysis algorithms were constructed to calculate the m6A score for each sample to quantify the m6A patterns. The patients in clusterB had higher m6A scores than those in clusterA. Furthermore, we found that the patients in clusterA were linked to helper T cell type 1 (Th1)-dominant immunity while those in clusterB were linked to Th2-dominant immunity. In summary, m6A regulators play nonnegligible roles in the occurrence of childhood asthma. Our investigation of m6A patterns may be able to guide future immunotherapy strategies for childhood asthma.

关键字 childhood asthma, m6A RNA methylation regulators, m6A-related genes, diagnostic biomarkers, consensus clustering

分类：23. Pulmonology 呼吸
1655

Clinical efficacy of Subcutaneous immunotherapy in children with allergic diseases

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Background: Allergic diseases, mainly including Atopic rhinitis (AR), Atopic asthma (AA) and Atopic dermatitis, are a class of diseases with tissue damage and/or organ dysfunction caused by abnormal immune response. In recent decades, the prevalence of allergic diseases has risen sharply, bringing a huge economic burden to the society. Allergic diseases are complex and multifactorial. Environment plays a important role in the occurrence and development of allergic diseases. Carrying out specific immunotherapy for specific allergens when conditions permit are very important for the prevention, treatment and prognosis of children's allergic diseases. This study retrospectively analyzed the efficacy and safety of subcutaneous specific immunotherapy in children who were allergic to dust mites and expected to provide data support for the clinical prevention and treatment of allergic diseases in children. Methods: 71 children with allergic rhinitis and/or allergic asthma whose skin prick test which was to detect dust mite allergen-specific was positive (++~++++) and received subcutaneous immunotherapy were selected. Asthma daytime symptom score, Asthma nighttime symptom score, Total nasal symptom score (TNSS), Medication score, Visual analogue scale score (VAS score), Fractional exhaled nitric oxide (FeNO), Peak expiratory flow variation rate, Forced vital capacity in predicted(FVC%pred), Forced expiratory volume in one second in predicted(FEV1%pred), Peak expiratory flow in predicted(PEF%pred), Maximal mid expiratory flow in predicted(MMEF%pred) were analyzed and compared before and after 6-month, 12-month, 24-month and 36-month treatment. Withdraw, adverse effects, and the changes of allergens were recorded. Results: 59 children(83.1%) completed the treatments. VAS score, Medication score, FeNO and PEF variation rate decreased as treatment continued among patients who completed the treatments. TNSS scores showed a trend of decline as treatment continued among children with rhinitis. Asthma daytime symptom score and Asthma nighttime symptom score showed trends of downward as treatment continued among children with allergic asthma. FVC%pred, FEV1%pred, PEF%pred and MMEF%pred showed trends of upward as treatment continued. Systemic Reactions occurred 71 times (2.81%) in 33 children (46.5%). SR mainly occurred in the maintenance treatment stage and 43 times (60.6%) SR occurred. Level I SR was the major adverse reaction and 48 times (48/71,67.6%) occurred. After SCIT the SI of dermatophagoides pteronyssinus and dermatophagoide farinae decreased. Conclusion: The control of asthma/rhinitis, medication score and pulmonary related indicators were improved after SCIT treatment. The SI of dermatophagoides pteronyssinus and dermatophagoides farinae after SCIT were lower than that before treatment. The incidence of systemic reactions of SCIT was low, and SCIT was of high safety.

关键字 Children; Allergic diseases; Subcutaneous immunotherapy

分类：23. Pulmonology 呼吸
1657

Step-down treatment in patients with asthma well-controlled by long-acting beta2-agonists(LABA) and inhaled corticosteroids(ICS): A meta-analysis

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Background: Step-down therapy is advocated when asthma is stable. Continuing combination ICS-LABA with a reduction in ICS/LABA component and discontinuing LABA are both options of medication strategies. But which strategy is better is not known. To identify randomized controlled trials (RCT) to compare the risk of asthma exacerbation between stable asthmatic individuals stopping LABA and individuals reducing ICS/LABA. Method: We searched several databases with no language restrictions. We included randomized controlled trials (RCTs) that evaluated the effect of step-down treatments in persons with asthma well-controlled by LABA and ICS. We included the studies of participants who reduced the dosage of ICS/LABA or unchanged the dosage of ICS(LABA step-off). Results: The search strategy revealed 3925 different records, of which 30 full-texts were assessed for eligibility. 9 studies met the criteria for inclusion. Nine included studies were randomized controlled trials. There was a significant difference in peak expiratory flow (PEF) (MWD, 18.86; 95% CI,10.95 to 20.77). We couldn't rule out the possibility that the persons who reduced ICS/LABA had fewer withdrawals and had fewer serious adverse events. But in terms of asthma exacerbation, serious adverse events, FeNO and ACT, the two step-down strategies had no significant difference. Conclusions: Although the data is limited, reducing ICS/LABA might be a better choice than stopping LABA. This review supported that stopping LABA in asthmatic patients may slightly reduce the PEF and increase the likelihood of withdrawals and the occurrence of serious adverse events, but this is not certain and longer trials are requisite.

关键字 Asthma; Step-down; Long-acting beta2-agonists; Inhaled corticosteroids.

分类：23. Pulmonology 呼吸
1663

Study on relationship between CARDS TX, TNF-α and hypercoagulable state in children with RMPP

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Abstract Objective To study the expressions of community-acquired respiratory distress syndrome toxin (CARDS TX) and tumor necrosis factor-α (TNF-α) in children with refractory mycoplasma pneumoniae pneumonia (RMPP), and to analyze their relationship with hypercoagulable state in children. **Methods** 90 children with RMPP in the hospital were selected as the RMPP group, and another 90 healthy children were enrolled as the control group. The levels of fibrinogen (FIB), D-dimer (D-D), activated partial thromboplastin time (APTT), prothrombin time (PT), CARDS TX and TNF-α were compared between the two groups, and the correlation between CARDS TX, TNF-α and coagulation indicators in children with RMPP was analyzed. The intrapulmonary and extrapulmonary complications were compared among RMPP children with different coagulation status, and different levels of CARDS TX and TNF-α. **Results** The levels of FIB, D-D, CARDS TX and TNF-α in the RMPP group were higher than those in the control group, and APTT was shorter than that in the control group (all $P<0.05$). Correlation analysis showed that CARDS TX and TNF-α in children with RMPP were positively correlated with FIB and D-D, and were negatively correlated with APTT (all $P<0.05$). The incidence rates of pleural effusion, atelectasis and skin rash in the hypercoagulable state group were higher than those in the non-hypercoagulable state group, and the incidence rates in the high-level CARDS TX group were higher than those in the low-level CARDS TX group, and the incidence rates in the high-level TNF-α group were higher than those in the low-level TNF-α group (all $P<0.05$). **Conclusion** The levels of CARDS TX and TNF-α are related to hypercoagulable state and intrapulmonary and extrapulmonary complications in children with RMPP.

关键字 Refractory mycoplasma pneumoniae pneumonia; Community-acquired respiratory distress syndrome toxin; Tumor necrosis factor-α; Hypercoagulable state

分类：23. Pulmonology 呼吸
1714

The association between ambient temperature and pediatric outpatient and emergency visits for asthma in Hangzhou, China

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Background: Asthma is a polygenic hereditary disease with a distinct tendency to flock. The external environment we are exposed to, such as allergens, atmospheric pollutants, meteorological factors, pathogenic microorganisms, are considered to be closely related to the occurrence and development of asthma. We aimed to identify the correlation of temperature and asthma exacerbation in Hangzhou, China.
Methods: We collected monthly average data of temperature and the outpatient and emergency visits of asthmatic children in the children's hospital of Zhejiang university school of medicine from 2014 to 2017. Correlation analysis was conducted between temperature and the visits of asthmatic children to explore the relationship between them.
Results: It was found that there was a negative correlation between ambient temperature and asthma visits, especially among children younger than 6 years of age.
Conclusions: Based on clinical observation, our study suggests that lower temperature was an environmental risk factor for asthma exacerbation, which is more pronounced in younger children.

关键字 asthma，temperature，outpatient and emergency visits

分类：23. Pulmonology 呼吸
1731

Study on Relationship Between Specific IgE and Polymorphisms of IL-4 -33C/T and IL-13 +1923C/T in 305 Asthmatic Children of Guiyang Area

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Objective:To investigate the single nucleotide polymorphisms (SNP) of -33 site in the promoter region of IL-4 gene,+1923 site in the intron-3 region of IL-13 gene and the susceptibility of asthma,and the association with (SIgE). Methods:305 asthmatic children (experimental group) and 200 healthy children (control group) were recruited. PCR-RFLP was used to detect the genotypes of IL-4 gene -33 site and IL-13 gene +1923 site. SIgE was measured by western blotting examination.Results:①The three genotypes of the IL-4-33C/T and IL-13 + 1923C/T sites were CC, CT, TT genotypes in both asthma and control groups, with statistically significant differences in the distribution of genotype frequencies between the two groups(P<0.01).②In asthma and control groups, the C allele frequency at IL-4-33C/T locus was 35.7% and 54.8% ,the T allele frequencies at the same locus was 64.3% and 45.2%, respectively.Besides,the C allele frequency at the IL-13 + 1923C/T site was 48.5% and 51.5%, respectively,the T allele frequencies was 65.8% and 34.2%, respectively.The allele frequencies at each locus had the significantly difference in asthma and control groups (P<0.01), the variant allele T carriers have higher risk of asthma.③Inhalational allergens on -33C/T locus of IL-4,the genotype frequency was significantly different between dust-mite-positive group, house-dust-positive group, dog-positive group and controls (P<0.01).The allele frequency was significantly different between the three groups and controls (P<0.01).The carriers with variant allele have a higher risk of dust-mite-positive group, house-dust-positive and dog-positive. ④Food allergens on -33C/T locus of IL-4,the genotype frequency was significantly different between abyssal fish group and controls (P<0.01). And this difference was also found in freshwater fish group,soybean group(P<0.05).The allele frequency was significantly different between freshwater fish group, abyssal fish group and controls (P<0.01).The carriers with variant allele have a higher risk of freshwater fish group and abyssal fish. ⑤Inhalational allergens on +1923C/T locus of IL-13,the genotype frequency was significantly different between dust-mite-positive group house-dust-positive group and dog-positive group and controls P<0.01)and this differencewas also found in cockroach group (P<0.05).The allele frequency was significantly different between the four groups and controls (P<0.01).The carriers with variant allele have a higher risk of dust-mite-positive, house-dust-positive,dog-positive and cockroach.⑥Food allergens on +1923C/T locus of IL-13,the genotype frequency was significantly different between freshwater fish group, abyssal fish group,crab group and controls(P<0.01).And this difference was also found in soybean group (P<0.05).The allele frequency was significantly different between freshwater fish group, abyssal fish group, crab group, soybean group and controls (P<0.01).The carriers with variant allele have a higher risk of freshwater fish group, abyssal fish group, crab and soybean (OR=2.510, 95%CI 1.576-3.998, OR=2.378, 95%CI 1.551-3.870, OR=2.967, 95%CI 1.352-6.511, OR=3.359, 95%CI 1.376-8.204).Conclusion: ① The T allele on -33 locus of IL-4 and on +1923 locus of IL-13 are associated with children asthma risk in GuiYang area. And the -33 of IL-4 and +1923 of IL-13 polymorphism sites are all important

candidate genes for children asthma in GuiYang area.②In the inhalant allergens ,the variant allele T of IL-4 -33 and IL-13 +1923 are risk factors for asthma children to be allergic to dust mite group,house dust and dog.And T of IL-13 +1923 is risk factor to cockroach.③In the food allergens,the variant allele T of IL-4 -33 and IL-13 +1923 are risk factors for asthma children to be allergic to freshwater fish group and abyssal fish group.And T of IL-13 +1923 is risk factor to crab and soybean.

关键字 asthma; interleukin-4; interleukin-13; SIgE; polymorphism

分类：23. Pulmonology 呼吸
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Clinical efficacy of SLIT in the treatment of asthma, asthma and allergic rhinitis in children

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Objective: To understand the effects of sublingual immunotherapy (SLIT) on symptom fractional exhaled nitric oxide (FeNO) levels, and lung function in children with asthma, asthma and allergic rhinitis, for SLIT treatment of childhood asthma, asthma and rhinitis provide clinical evidence. Methods: The children who were diagnosed with bronchial asthma and allergic rhinitis diagnosed at the Children's Respiratory Specialist Clinic of the Affiliated Hospital of Guizhou Medical University and the Department of Otorhinolaryngology were selected,skin prick tests or serum to detect dust mite allergen-specific positive (sIgE:++and above);treatment in Children's respiratory specialist, otolaryngology department and diagnosed as bronchial asthma(BA), allergic rhinitis(AR) in children, 91 children with bronchial asthma, 54 children with bronchial asthma and rhinitis, skin prick test or serum-specific allergen test dust mite positive, drug therapy alone for the inhaled corticosteroid(ICS) group, with parental consent for drug treatment combined with SLIT treatment for the ICS+SLIT group; record the clinical manifestations of children, with or without acute asthma attack, β-2 receptor agonist use, children review nitric oxide,pulmonary function.Independent sample t test was used for age comparison, and chi-square test was used for gender comparison. FeNO level and lung function were compared by anova at different time points in children with asthma and those with asthma with rhinitis, and LSD test was used for pairwise comparison.ICS group was compared with ICS+SLIT using independent sample t test. Results: ①There was no significant difference in age and sex between ICS group and ICS+SLIT group(P>0.05).②FeNO levels: FeNO levels in children with ICS and ICS+SLIT decreased compared with those before treatment, and FeNO levels decreased significantly in children with ICS+SLIT (P<0.05).There was no significant difference between the ICS group and the ICS+SLIT group in children with asthma，asthma with rhinitis (all P>0.05). The level of FeNO in children with asthma with rhinitis was higher than that in children with asthma alone.③Pulmonary function: The indexes of lung function in children with ICS and ICS+SLIT were improved compared with those before treatment. Compared with ICS group, the ICS+SLIT group had significant improvement in lung function FVC treatment for 9 months, and PEF treatment for 12 months were significant improvement, FEF25 treatment for 12 months was statistically significant (P<0.05). The lung function indexes of ICS group and ICS+SLIT group in asthma with rhinitis were improved compared with those before treatment.Compared with ICS group, the ICS+SLIT group of lung function index FVC for 9 months and treatment at 12 months had significant improvement. The difference was statistically significant. (P<0.05); The lung function index of lung function was significantly improved first; the lung function value of ICS+SLIT group was higher than that of ICS group in children with asthma, asthma and rhinitis. The index of lung function of asthmatic children was higher than that of asthmatic children with rhinitis.Conclusion:①ICS therapy can improve clinical symptoms, reduce drug use, reduce FeNO levels, and improve lung function;②ICS combined with SLIT treatment can significantly improve clinical symptoms, reduce drug use, reduce FeNO levels, and improve lung function; ICS+SLIT group FeNO level, lung function than ICS alone. ③SLIT treatment is a safe and

effective treatment. Long-term, adequate SLIT treatment can improve patients' symptoms, better control disease progression and improve quality of life.

关键字 Bronchial asthma; allergic rhinitis; children; sublingual immunotherapy; dust mites

分类：23. Pulmonology 呼吸
1773

The clinical application of flexible bronchoscopy in the diagnosis and treatment of chronic cough in children

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Objectives: Chronic cough is a common symptom in children. It is difficult to diagnose chronic cough by detailed history, physical examination and conventional auxiliary examination for the reason that chronic cough has complex diversity of clinical manifestations and causes. In recent years, flexible bronchoscopy has been widely used in pediatrics. The objective of the study was to explore the clinical application of flexible bronchoscopy in the diagnosis and treatment of chronic cough in children.
Methods: 211 cases of children with chronic cough who needed to receive flexible bronchoscopy for diagnosis and treatment in the Respiratory Department of Children's Hospital of Zhejiang University School of Medicine from October 28, 2019 to May 28, 2021 was selected. Retrospectively analysis etiology and clinical menifestation, the pathogens in bronchoalveolar lavage fluid.
Results: In the 211 patients, 127 cases were males (60.2%) and 84 cases were females (39.8%). 106 cases (50.2%) were caused by upper airway cough syndrome, 56 cases (26.5%) by post-infection cough, 54 cases (25.6%) by gastroesophageal reflux and throat reflux, 39 cases (18.5%) by cough variant asthma, 36 cases (17.1%) by respiratory tract dysplasia, 23 cases (10.9%) by protracted bacterial bronchitis, 19 cases (9.0%) by bronchial foreign body, 6 cases (2.8%) by bronchial tuberculosis, 4 cases (1.9%) by recurrent respiratory tract infections, 3 cases (1.4%) by primary ciliary dyskinesia, 6 cases (2.8%) by bronchiolitis obliterans, 2 cases (0.95%) by obliterative bronchitis, 9 cases (4.3%) by other rare diseases (1 case by necrotizing pneumonia, 2 cases by Kartagener syndrome, 1 case by bronchial atresia, 1 case by psychogenic cough, 1 case by obstructive sleep apnea syndrome, 1 case by SP-C gene defect, 1 case by cystic fibrosis, 1 case by pertussis syndrome). All 211 cases were performed with bacterial culture of bronchoalveolar lavage fluid (BALF), 60 cases were positive (28.4%). 33 samples were streptococcus pneumoniae (15.6%), which was the most common pathogen, 14 samples were mycoplasma pneumoniae (6.6%) and 12 samples were haemophilus influenzae (5.7%). Cytology examination of BALF showed the percentage of neutrophil cells was significantly higher in the PBB group than in other groups ($P<0.05$).
Conclusions: The causes of chronic cough in children are complex and have individual differences. This study found that upper airway cough syndrome was the most common cause of chronic cough in children, which accounts for about half. Post-infection cough,
gastroesophageal reflux and throat reflux, cough variant asthma, respiratory tract dysplasia and protracted bacterial bronchitis were also the main causes of chronic cough in children. Streptococcus pneumoniae, Mycoplasma pneumoniae, and Haemophilus influenzae were the main pathogens of chronic cough. Flexible bronchoscopy had obvious advantages in the detection of congenital respiratory tract dysplasia, discovery and removal of bronchial foreign body, removal of sputum and mucus plug in bronchi, diagnosis of protracted bacterial bronchitis, and confirming pathogen. For the chronic cough children who had repeated visits and poor treatment can select flexible bronchoscopy examination for diagnosis and treatment.

关键字 flexible bronchoscopy,chronic cough,children,diagnosis,treatment

分类：23. Pulmonology 呼吸
1801

The association between the level of plasma D-dimer and disease severity and prognosis of Mycoplasma pneumoniae pneumonia in children

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Objective: To explore the association between the levels of plasma D-dimer and disease severity and prognosis of Mycoplasma pneumoniae pneumonia (MPP) in children Methods: We retrospectively analyzed data of MPP patients who were hospitalized in our hospital between January 1, 2016 and December 31, 2018. According to the peak value of D-dimer, patients were divided into the normal group (D-dimer<0.55mg/L) and the elevated group (D-dimer≥0.55mg/L). The demographic and clinical information, auxiliary examination, treatments and outcomes of patients were compared. Results: Of 231 MPP patients, 80 patients were in the normal group, 161 patients were in the elevated group. The age of patients in D-dimer elevated group was significantly higher than that in normal group (P<0.01). Comparing with the normal group, longer length of fever, hospital stay and antibiotic therapy, more severe radiographic manifestations were found in the elevated group (P<0.01). Meanwhile, the incidence of extrapulmonary complications, refractory MPP and severe MPP in the elevated group were significantly higher than those in the normal group (P<0.01). As to the laboratory data, we found that neutrophils (P<0.01), C-reactive protein (P<0.01), lactate dehydrogenase (P<0.01), interleukin-6 (P<0.05), interleukin-10 (P<0.01) and interferon-γ (P<0.01) were significantly higher in the elevated group than those in the normal group. After treatments, all patients were discharged without death, but the proportions of patients requiring glucocorticoid (P<0.01), bronchoscopy (P<0.01), thoracentesis (P<0.05) were significantly higher in the elevated group than those in the normal groups (P<0.01). Follow-up study showed that in the absorption rate of lung lesions at 4 weeks after admission was significantly higher the time for lung lesions absorption was significantly shorter and the incidence of pulmonary sequelae was significantly lower in the normal group than those in the elevated group (P<0.05). Correlation analysis showed that D-dimer level was positively correlated with the severity of pneumonia and the occurrence of pulmonary sequelae. In ROC curve analysis, the cut-off value for the D-dimer was set at 0.82mg/L. Conclusions: MPP children with elevated plasma D-dimer are more likely to have severe clinical manifestations, longer duration of treatment, longer recovery time for lung lesions, and the possibility of pulmonary sequelae.

关键字 Children, Mycoplasma Pneumonia, Pneumonia, D-dimer

Infectious Disease

感染

Category: 15. Infectious Disease 感染
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A case of neonatal sepsis caused by Coxsackie B1 virus infection and literature review

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Abstract Content To summarize the clinical characteristics of a case of neonatal sepsis caused by Coxsackie (COX) B1 virus infection and review the related literature.
Methods To describe the clinical data of a case of neonatal sepsis caused by Coxsackie B1 virus infection in the author's unit, and search the Chinese database (Chinese National Knowledge Infrastructure database, Wanfang Database) with "newborn" and "Coxsackie virus infection" as search terms; using "neonate/Coxsackievirus Infections" and "neonatal coxsackievirus" as English search terms, search Pubmed and Google Scholar databases from January 2010 to December 2020 for literature review.

Results The main manifestations of this newborn were DIC and multiple organ dysfunction. The metagenomic next generation sequencing of peripheral blood infectious pathogens showed Coxsackie type B1, and the child recovered after treatment. Through literature review and combined with this case, a total of 61 newborns were found. The incidence within 7 days after birth was 83.01%; the male to female ratio was 1.4:1; the main clinical manifestations were respiratory distress, feeding difficulties, poor peripheral perfusion, fever, hepatomegaly, and arrhythmia; the main diagnosis was viral myocarditis, viral brain Inflammation, multiple organ dysfunction syndrome, viral hepatitis, myocardial damage, pneumonia, sepsis, DIC, necrotizing enterocolitis, hemophagocytic lymphohistiocytosis;the incidence of organ damage from high to low is heart, brain, liver, lung, and kidney damage related reports have not been collected;the most common neonatal Coxsackie virus is group B Coxsackie virus (CXB), which can cause disease from CXB1 to CXB5 subtypes. CXA infection is occasionally seen. CXB3 and CXB5 are the main epidemic virulence serotypes of CXB, each accounting for 32.69%; 45 cases were cured, 16 cases died, and the mortality rate was 26.23%. Among them, 11 cases died from multiple organ dysfunction, and 10 cases died from CXB3, which were the most important causes of death.

Conclusion Neonatal coxsackievirus infection is characterized by long course of disease and atypical clinical manifestations, which can affect every organ system in the whole body. Vertical transmission may be the most important source of infection. The prognosis of the disease depends on the serotype and the number of organ dysfunction.

Key words Coxsackie virus; neonatal sepsis; mNGS
Reference

Category: 15. Infectious Disease 感染
18

Severe pneumonia caused by H1N1 influenza in children with peripheral blood eosinophilia and literature review

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Abstract Content To summarize the clinical characteristics of a case of H1N1 influenza virus infection with peripheral blood eosinophilia and literature review.
Methods Describe the clinical data of a case of H1N1 influenza virus infection with peripheral blood eosinophilia in our hospital , and search the Chinese database(China National Knowledge Infrastructure, Wanfang database) with "influenza virus" and "eosinophilia" as search terms until November 2020; using "eosinophil/influenza" and "hypereosinophilia/influenza" as search terms, search Pubmed and Google scholar databases from January 2000 to November 2020 about H1N1 influenza virus infection with peripheral blood eosinophilia, and review the literature.
Results A total of 0 Chinese literature and 8 English literatures were retrieved. Combined with this patient, a total of 53 patients were found. 47 patients with H1N1 infection and peripheral blood eosinophilia all showed severe pneumonia; 6 patients were vaccinated with influenza, and patients with peripheral blood eosinophilia all showed hypersensitivity; there was no increase in alveolar eosinophilia in 7 patients with H1N1 influenza virus pneumonia ; 43 cases (81.1%) with mild eosinophilia, 7 cases (13.2%) with moderate increase, 3 cases (5.7%) with severe increase; 53 patients were cured after reasonable treatment, and the cure rate was 100%.
Conclusion: Eosinophilia is closely related to H1N1 influenza virus infection and influenza vaccination; peripheral eosinophilia may be a protective response to severe pneumonia caused by H1N1 influenza, and eosinophilia and alveolar eosinophilia may be Irrelevant; the increase in eosinophils caused by artificial autoimmunity is caused by hypersensitivity. The main treatment for severe pneumonia is oseltamivir, and hypersensitivity requires anti-inflammatory and anti-allergic treatment.

Key words H1N1 influenza virus; eosinophilia; eosinophils
Reference

Category: 15. Infectious Disease 感染
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Clinical distribution characteristics and drug resistance analysis of multidrug-resistant bacteria in a hospital

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Abstract Content To summarize and analyze the distribution of multidrug-resistant bacteria and their antimicrobial resistance in our hospital, and to grasp the distribution trend of multidrug-resistant bacteria in time, so as to provide effective reference for rational use of antimicrobial agents.

Methods The multidrug-resistant bacteria detected in various specimens (such as pus, urine, sputum, blood, deep respiratory secretions, etc.) of 365 children hospitalized in Xi 'an Children's Hospital from January 1 to December 31, 2020 were analyzed retrospectively by pathogen detection and drug sensitivity test.

Results Results A total of 365 strains of multidrug-resistant bacteria were detected, and the distribution of strains was most common in surgical wards, followed by intensive care wards and respiratory medicine wards The main strains detected were Escherichia coli, Staphylococcus aureus and Klebsiella pneumoniae. Among the positive specimens, pus, urine, sputum and blood are the most common. Among the 365 strains, 94 strains were Gram-positive bacteria (G+ bacteria), accounting for 25.75%; There are 271 gram-negative bacteria (G-bacteria), accounting for 74.25%. The drug resistance rates of Escherichia coli and Staphylococcus aureus were 47.67% and 25.21%, respectively. The drug resistance rate of Klebsiella pneumoniae was 10.96%. The drug resistance rate of Klebsiella oxytoca was 2.19%. The resistance rate of Acinetobacter baumannii to carbapenems (such as meropenem) was 9.32%. Two cases of Enterococcus faecalis resistant to vancomycin were detected in this strain (resistance rate < 1%).

Conclusion The monitoring of bacterial drug resistance is still the focus of clinical treatment, and we should pay attention to pathogen examination to guide the rational use of antibiotics in clinic. Most of the patients with multidrug-resistant bacteria were children with surgical diseases, so hospitals should strengthen isolation management and monitor drug-resistant bacteria.

Key words Multidrug-resistant bacteria; Drug resistance; Antibacterial drugs; measure
Reference

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Characteristics of S. pyogenes isolated from Chinese children with different diseases

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Abstract Content Background *Streptococcus pyogenes* is an exclusive human bacterial pathogen, which can cause a wide spectrum of clinical diseases and ranks first among the top ten causes of death from infectious diseases in the world. The drug resistance of *S. pyogenes*, the relationship among the *emm* gene and the virulence gene spectrum, and disease types were affected by temporal changes and geographical location, and are also hotspots in global microbial research. In order to analyze the epidemiological characteristics of *S. pyogenes* strains in Shenzhen, China from 2016 to 2018, 342 strains isolated from children with different diseases were included in this study.

Methods Antimicrobial susceptibility tests were performed as recommended by CLSI. The ermB, ermA, mefA, and tetM, emm gene, and 13 sAgs were detected by PCR. Forty-two representative strains (21 each from emm1.0 and emm12.0) isolated from patients with scarlet fever or obstructive sleep apnea-hypopnea syndrome were subjected to whole-genome sequencing and assembly, gene annotation, and phylogenetic analysis, and analyzed the antimicrobial susceptibility to vancomycin.

Results All strains were universally susceptible to penicillin and chloramphenicol, and resistant to macrolides (>90.0%, 256μg/mL) and tetracycline (86.5%, >64μg/mL). Percent 90.9% macrolides resistance strains harbored the ermB and 85.4% tetracycline resistance strains harbored the tetM. Ten *emm* genotypes, including 7 subtypes, were identified. The most prevalent *emm* genotypes were *emm*12.0 (58.8%), *emm*1.0 (30.7%). Percent 79.5% strains carried six or more sAgs. Five major gene profiles (A-E) were identified. The distributions of *emm* genotypes and sAgs were not significantly different in disease types. The distribution of *speA, speH, speI, speJ,* and *ssa* varied among *emm* types; *speL* in *emm*12.0 strains between bronchitis and scarlet fever and between obstructive sleep apnea-hypopnea syndrome and scarlet fever; and *ssa* in *emm*12.0 strains between invasive and noninvasive was significantly different. Among 42 representative strains, all strains were susceptible to vancomycin. The *pbp2x, bcrA, bacA, pmrA, lmrP, vanB* and *vanrG* were present in all strains. The *vanuG* was present in 64.3% strains, and the carrier frequency in *emm*12.0 (18/21) was significantly higher than that in *emm*1.0 (11/21) . The *bcrA* was a double copy gene, and the remaining nine drug resistance genes were single copy. The *prtF1, prtF2, sfbII, sfbX, hlyD*, and *fbp54* and *speG, speH*, and *speI* were conserved and unique to emm12.0, whereas the *CPF_2072, fbaA, fctA, fctB, mf3, and fbpA,* and *speA, speG,* and *speJ* were conserved and unique to *emm*1.0. The frequency of *sda* was significantly higher in *emm*12.0 (20/21) than in *emm*1.0 (15/21). Two copies of *hylP* were mainly distributed in the *emm*1.0, and three copies of *hylP* were distributed in the *emm*12.0 .

Conclusion Most strains mainly harbored the *ermB* and *tetM*. The rates and levels of resistance to macrolides and tetracycline were high. The most prevalent *emm*12.0 and *emm*1.0 had one stable genetic clone each. The *emm* genotypes was not correlated with

disease. The sAgs, vanuG, and virulence genes were associated with *emm* genotypes but not with disease.

Key words S. pyogenes, Disease, China, Child, Superantigen, emm genotype, Antibiotic resistance

Reference

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Analysis of the risk factors for death caused byof infants with carbapenem-resistant Klebsiella pneumoniae bloodstream infection in infants

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Abstract
Background
Carbapenem-resistant Enterobacteriaceae (CRE) are on the rise worldwide. Due to the limited treatment options and high morbidity and mortality, infections caused by CRE are a serious public health problem . Although the isolation rate of multidrug resistant (MDR) strains has decreased in the past 10 years, the isolation rate of CRE has increased to 3.9%, especially in pediatrics departments and intensive care units (ICUs), according to the 2014 National Drug Resistance Surveillance Network in China . Another study reported catheter-related bloodstream infections with an overall 30-day mortality rate of 45% as the most frequent infection among these patients .
Thus, understanding the risk factors for death associated with infections, such as those caused by CRE, could be useful in directing therapeutic resources in high-risk patients and planning interventions targeting risk factors that could reduce mortality. Understanding the risk factors for death caused by CRE could be useful in designing therapeutic interventions directed to CRE-infected patients. In this study, we assessed the risk factors for death caused by carbapenem-resistant Klebsiella pneumoniae (CRKP) bloodstream infection in pediatric emergency and critical care units.
Methods
A total of 42 CRKP-infected children who were admitted at the Xinhua Hospital, Shanghai Jiaotong University School of Medicine between January 1, 2017 and December 30, 2019 were enrolled in this study. Demographic characteristics, basic clinical data such as invasive procedures performed before infection, and other general data were collected. ANOVA and multiple logistic regression analyses were used. Regression analysis was used to explore the risk factors of CRKP death.
Results
Univariate analysis showed that there were statistically significant differences in the basic clinical data (i.e. birth status at delivery (i.e. premature or full-term), parenteral nutrition) and invasive procedures (i.e. surgery, tracheal intubation and central venous catheterization) performed on the children ($P<0.05$). Multivariate analysis showed that central venous catheterization, birth status at delivery, and surgery were independent risk factors for death.
Conclusion
The risk factors for death caused by CRKP in infants mainly include invasive procedures (i.e. surgery, tracheal intubation), central venous catheterization, parenteral nutrition, and birth status at delivery. In particular, surgery and central venous catheterization were independent risk factors for death. Our results suggest that these risk factors should be targeted in therapeutic interventions for CRKP.

关键字 Carbapenem-resistant Klebsiella pneumoniae, bloodstream infection, risk factors for death

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A small number of acute lower respiratory tract infection in children in China is associated with enterovirus D68 infection

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Methods：The 3071 children patients were from a multicenter study including 7 hospitals of 6 provinces (Beijing, Ningxia, Zhejiang, Liaoning, Guizhou, Guangdong). Inclusion criteria: younger than 18 years old, diagnosed as acute lower respiratory tract infection. The specimens including nasopharyngeal swabs and sputum to screen by polymerase chain reaction(PCR) assay were collected. Viral nucleic acid was extracted by QIAamp MinElute Virus Spin Kit. All specimens were detected by Multiplex Real-time PCR Diagnostic Kit Rapid Detection of 16 Species of Respiratory Pathogens. The enterovirus positive specimens were further tested by EV-D68 nucleic acid detection real-time PCR kit. EV-D68 positive specimens were performed on VP1 gene sequencing. The isolated EV-D68 strains were performed on the whole genome sequencing. The viruses were isolated from clinical samples and cultured in Rhabdomyosarcoma(RD) cells. RD cells were maintained in high-glucose Dulbecco’s modified Eagle’s medium supplemented with 10% fetal bovine serum. The SH-SY5Y cells were maintained in a 1:1 mixture of DMEM and F-12K medium supplemented with 10% FBS.

Results：Among 3071 specimens, ten EV-D68 positive specimens were detected (4 cases from Zhejiang province and 6 cases from Ningxia province). The annual detection specimens of EV-D68 were 1/485 in 2017, 9/1518 in 2018 and 0/1068 in 2019. Four EV-D68 strains (YC17106/NX/CHN/2017, YC18116/NX/CHN/2018, YC18137/NX/CHN/2018, WZ17226/ZJ/CHN/2018) were isolated. Ten VP1 sequences and 4 complete genomes were successfully obtained.
The median age of 10 EV-D68 patients was 32.7 months old (5-92m). Nine (90%) patients were male and 1(10%) patient was female. Most of children were admitted to the hospital in the summer and autumn. Among 10 EV-D68 patients, 8 patients (80%) were diagnosed with pneumonia and 2 patients (20%) with bronchiolitis. No case was diagnosed with severe pneumonia and admitted to the ICU ward. No clinical syndrome of nervous system was found. All the cases had no history of asthma or immunodeficiency. The patients were all cured and discharged from hospital. No epidemiological linkage was found among 10 patients.
The phylogenetic tree of VP1 genes showed that EV-D68 strains could be divided into 4 clades (A-D). All Strains in this study belong to subclade B3.
SH-SY5Y is a “neuronal-like” cell line drevied from neuroblastoma. David et al. was successful to used it as a cell model to identity the neurotropism of EV-D68 strains. The EV-D68 isolate WZ17226 in this study was used to infect “neuronal-like” cell line SH-SY5Y and cytopathic effect was observed. The viral titer was determined in ~104.4TCID50/ml in SH-SY5Y cells. The infection experiment showed that the strains in China also had the ability to infect neuronal cell line SH-SY5Y.
There was a study showed that 6 AA substitutions(M291T, V341A, T860N, D927N, S1108G and R2005K) related to neurovirulence were found in subclade B1 AFP strains. In this study, these 6 AA substitutions were indeed found in subclade B1 AFP strains in 2014 but not in our four subclade B3 strains, subclade B3 AFP strains in 2016 as well as

the subclade B1 AFP strain in the USA in 2013. Secondly, the noncoding region was analyzed. There were three mutations positions in 5' UTR(127T, 262C, 339T) of subclade B1 strains and other AFP-causing enteroviruses such as EV-D70. But these three nucleotide substitutions were also not observed in our four strains and subclade B3 AFP strains. The 3' UTR may form a pseudoknot structure in all 2014 Chinese strains but not in 2014 American strains. We found that this structure could also be observed in our four 2018 strains and 2016 American subclade B3 AFP strains. These results suggested that these existing differences in complete genome may not be enough to explain the neurovirulence of EV-D68.

关键字 Enterovirus D68, China, Infection, Genome analysis, Neurotropism

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The basis of α-hemolysis negative Methicillin-resistant Staphylococcus aureus isolates from Beijing Children's Hospital

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Abstract

Background. Methicillin-resistant Staphylococcus aureus (MRSA) Clonal Complex 59 (CC59) clone has spread among Chinese children, resulting in many Staphylococcus aureus infections. α-hemolysin (Hlα) is an important virulence factor of Staphylococcus aureus, but little research has been done on CC59 isolates with negative α-hemolysis.

Results. During the 4 periods (2009-2011, 2012-2013, 2016, 2017), 291 MRSA isolates were collected. Isolates with β and δ hemolysis accounted for 60.47% among the MRSA isolates in 2009-2011; 56.41% in 2012-2013; 77.14% in 2016; and 56.25% in 2017. most ST59 isolates (94.38%), 9 ST338 isolates (100%) showed β and δ hemolysis, both ST59 and ST338 clone belong to CC59 clone. Twenty-two ST239 isolates (73.33%), 8 ST88 isolates (80%), 4 ST5 isolates (100%), 13 ST22 isolates (92.86%) and 6 ST398 isolates (85.71%) showed α and δ hemolysis. α hemolysin in most clinical isolates is highly conservative, each showed one amino acid locus variation, the most common mutation was threonine at position 275 instead of isoleucine, then glutamic acid replaced aspartic acid at 208. Seventeen ST59 and 2 ST338 isolates had no mutation, 3 ST59 isolates showed single mutation (C448G), and only one ST59 isolate showed multilocus mutation. Other ST typing, such as ST1, ST5, ST88, ST20, ST239 and ST398, all had multilocus mutations, sites were from 3 to 8, no conservative sequence was found among isolates with the same ST typing. The carrying rates of RNA III, Rot, agrA, SarR, SarU and SigB were all over 93%, the carrying rates of SarZ and SarA genes were 41.86% and 34.88% respectively. Trancriptional levels of hlα in isolates showed α and δ hemolysis and β and δ hemolysis were equal. USA300 and R23 produced Hlα, R23 didn't showed α hemolysis phenotype.

Conclusions. Most clinical CC59 isolates from children in China were α hemolysis negative. There was no statistically significant difference in hlα gene and RNA expression, they produced the protein. The reason for the phenotypic deletion probably related to β hemolysin (Hlβ).

关键字 Methicillin-resistant Staphylococcus aureus; ST59 clone; α-hemolysis; Children

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Prevention of Infant Morbidity Based on the Compliance of Intensive Breastfeeding Information Dissemination to Pregnant Mothers in Certain Communities in Bacolod City: A Cross Sectional Study

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Abstract Content Background: Despite overwhelming evidence of the benefits of exclusive breastfeeding, a small percentage of infants younger than six months are exclusively breastfed due to lack of understanding of optimal feeding practices and lack of support from health service providers, community members, and families. Breastfeeding can save the lives of both mothers and babies, this is one of the important interventions to reducing child morbidity and mortality.

The main objective of the study is to determine the impact of intensive breastfeeding information dissemination among pregnant mothers on its ability to prevent infant morbidity and sustain exclusive breastfeeding during the first six months.

Methods This is a cross sectional study conducted at Brgy. Villamonte and Brgy. Banago, Bacolod City. A total of 254 pregnant mothers on their third trimester were recruited. Participants were asked to answer a questionnaire prior to the intensive information dissemination, after attending three mothers' class, and at one, third, and six months postpartum. All participants received intensive counselling on breastfeeding in the form of brochures, pamphlets, lecture and video presentation weekly at least three weeks by the investigator and barangay health workers. Postnatally, subjects were monitored on the first, third, and sixth months on their ability to initiate and sustain exclusive breastfeeding as well as monitor for the presence or absence of infant diseases.

Results There was an increase in the average scores of the participants before and after intervention. A mean score of 33.8 with a standard deviation of 8.1 during the initial visit and a mean score of 36.9 with a standard deviation of 4.8 after the third visit implies that there is a significant difference on the knowledge on breastfeeding of mothers. Majority of the mothers at 78.3% were able to sustain exclusive breastfeeding for six months. Among the 21.7% who introduced breast milk substitute, majority was composed of formula milk at 76.4%. There is no significant relationship on the exclusive breastfeeding of mothers to the development of infant disease on the first month of life. However, as the study progresses to third and sixth months of life, it showed that there is a significant relationship between exclusive breastfeeding and the development of infant diseases with acute respiratory tract infection being the most common at 62.7% followed by diarrhea, otitis media, allergy, bronchial asthma, and constipation.

Conclusion Majority of the mothers were able to sustain exclusive breastfeeding for the first six months after intensive breastfeeding information dissemination. There is a significant relationship between exclusive breastfeeding and the development of diseases which implies that mothers who exclusively breastfed their children

for the first six months are at a lower risk of acquiring various diseases most especially acute respiratory tract infections as compared to those who introduced breast milk substitutes.

Key words intensive breastfeeding information dissemination, exclusive breastfeeding, infant morbidity, cross sectional study

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Clinical characteristics of human parvovirus B19 infection after congenital heart disease surgery

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【Abstract】Objective To summarize the clinical characteristics, treatment and prognosis of human parvovirus B19(HPV-B19) infection in children with congenital heart disease (CHD) after operation. Methods To retrospectively analyze the clinical manifestations, diagnosis and treatment of HPV-B19 infection after CHD operation diagnosed in Pediatric Intensive Care Unit (PICU) of Guangdong Provincial People's Hospital from June 2019 to June 2021. Results All the 10 children developed fever, mainly hyperpyrexia, without obvious poisoning symptoms, accompanied by sudden aggravation of anemia; 2 cases of diffuse congestive rash of trunk; 4 cases were mild anemia and 6 cases were moderate anemia. 4 cases were leukopenia, 2 cases were agranulocytosis and 1 case was granulocytopenia. Thrombocytopenia in 5 cases; 1 case of pancytopenia; Bone marrow hyperplasia decreased in 3 cases and erythroid hyperplasia decreased in 3 cases. The positive reaction was detected by quantitative polymerase chain reaction (qPCR) respectively from 7～23.0d days(average 12.8d days) after operation . 9 cases received intravenous injection of gamma globulin (IVIG) at an infusion volume of 300~700mg·kg-1·d-1 (mean 466.7mg·kg-1·d-1) for 2~5 days, and the other patient only needed transfusion of concentrated red blood cells and symptomatic treatment. The fever decreased within 2 ~ 9 days (mean 4.4 days) in 8 cases after the treatment of IVIG, platelets returned to normal in 3 cases from 2 to 7 days (mean 4.3 days), white blood cells returned to normal in 4 cases from 3 to 8 days (mean 5.3 days), hemoglobin gradually recovered in 4 cases from 5 to 17 days (mean 12.5 days), and hemoglobin concentrate did not decrease in 5 cases before infusion of IVIG. The HPV-B19 viral load was dynamically detected in 8 cases from 7 to 23d (mean 13.0d). QPCR analysis showed that the copy number of HPV-B19 decreased in 7 cases after the application of IVIG, decreased to 0copies/mL in 1 case, and still increased in 1 case before the application of IVIG. 9 cases were cured and discharged, and 1 case died of cardiogenic shock. Conclusion Early unexplained fever with leukopenia and anemia aggravation after CHD operation in children should be alert to infection with HPV-B19. Early use of IVIG after diagnosis can help promote recovery.

关键字 Congenital heart disease; Virus; Human parvovirus B19; infection

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Clinical Characteristics and Molecular Epidemiology of Methicillin-resistant Staphylococcus aureus infection in Children's Intensive Care Unit

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Objective To analyze the clinical characteristics of Staphylococcus aureus infection in the children's intensive care unit (ICU) in this region, to explore the risk factors of Methicillin-resistant Staphylococcus aureus (MRSA) infection in pediatric ward, and to analyze the resistance and virulence gene carrying status for MRSA.
Methods ⑴Retrospective analysis of medical records on infection in patients with Staphylococcus aureus children intensive care unit during 3 years was conducted. Univariate analysis and multivariate logistic regression were used to analyze the risk factors including age, gender and 17 other clinical related factors.⑵The bacterial identification was performed with VITEEK-2.⑶The Kirby-Bauer method was used to test the strain's drug resistance to pediatric commonly used antibiotics.⑷The broth microdilution method was used to detect MRSA's minimum inhibitory concentration(MIC).⑸Polymerase chain reaction (PCR) method was performed to detect the prevalence of the gene mecA, sea and seb, PVL, hla and hlb, agr1-4, eta and etb in MRSA.⑹Molecular typing of MRSA by bacterial molecular typing methods including staphyloccal protein A gene polymorphism, pulsed field gel electrophoresis (PFGE) and multilocus sequence typing (MLST).
Results ⑴There were 102 cases of Staphylococcus aureus infection in this study. Overall, 64.7% of cases were birth-1 years old, 61.7% were diagnosed with pneumonia, and the mortality rate was 9.8% (10/102).⑵Univariate analysis showed that gastric tube, suction, endotracheal intubation/incision, ventilator, catheterization, antibiotic use(≥3types), antibiotic use time (≥2 weeks), immunosuppressant/hormone, gamma globulin and hospitalization time (≥30 days) were closely related to the occurrence of MRSA infection. Noninvasive logistic regression analysis showed that mechanical endotracheal intubation /incision therapy, ventilator therapy and antibiotic use were all the independent risk factors of MRSA infection in children.⑶A total of 102 Staphylococcus aureus isolates were identified. The isolation source of sputum accounted for 59.8%, followed by nasal swab and throat swab, accounting for 21.6% and 9.8%.⑷Up to 38 (37.3%) isolates were proved to be MRSA. The resistance rates for common antibiotics in MRSA were erythromycin(92.1%), clindamycin(94.7%), streptomycin(52.6%), gentamicin(26.3%), sulfamethoxazole(5.3%) , respectively. ⑸The carrier rates for following virulence genes in MRSA were found: sea (47.4%), seb (47.4%), hla (97.4%), hlb (76.3%), agr1 (42.1%), agr2 (2.6%), agr3 (10.5%), and PVL (21.2%). Others gene like agr4, eta, etb and tst were not detected. The ioslates with two types, three types, four types, and five types of virulence genes accounted for 21.1% (8/38), 26.3% (10/38), 34.2% (13/38), and 15.8% (6/38) of all MRSA isolates, respectively.⑹Spa polymorphism analysis results showed, a total of 7 spa types in 38 MRSA, mainly t172 (15 strains, 39.5%), followed by t437 (10 strains, 26.3%).⑺PFGE results showed that 35 MRSA (3 isolates failed) were classfied into two clusters: cluster 3 (25/35) (similarity> 80%) and cluster 4 (6/35) (similarity> 85%), and four sporadic strains.⑻MLST typing results showed that 38 MRSA could be classified into 6 ST types, the dominant type being ST59 (n = 31, 81.6%). No new STs were found.

Conclusions ⑴The detection rate for MRSA in Staphylococcus aureus infection was 37.3% in this study.⑵The emergence of MRSA was caused by multiple factors, including mechanical tracheal intubation / incision therapy, ventilator therapy and multiple antibiotic use which were independent risk factors for MRSA infections.⑶Clinical isolation of drug-resistant Staphylococcus aureus is common.⑷Virulence gene detection results demonstrated that virulence genes in MRSA were complex. Most strains contained multiple virulence genes.⑸Molecular biology studies showed that ST59-t172 (39.5%) and ST59-t437 (26.3%) were prevalent strains, ST-59 MRSA were dominantly detected (81.6%).

关键字 NICU&PICU; methicillin-resistant Staphylococcus aureus; clinical features; drug resistance; molecular epidemiology

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Clinical study of acute lower respiratory tract infection caused by respiratory syncytial virus in neonates

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Objective: Exploring the clinical characteristics of acute lower respiratory tract infection (ALRTI) caused by respiratory syncytial virus (RSV) in neonates and to analyze the risk factors and early warning factors in severe infection. Methods: (1) To analyze the clinical data of 399 cases of neonatal ALRTI, which RSV nucleic acid or RSV antigen were positive. The cases were diagnosed from January 2014 to December 2020 in the neonatology department of Shenzhen Children's Hospital. The severity of RSV infection was evaluated by severity index (SI) , dividing the cases into two groups called severe infection group and mild and moderate infection group. To compare the clinical data of the two groups, and the multivariate logistic regression analysis were performed to analyze the risk factors and early warning factors in severe RSV infection. Results: (1) A total of 399 cases were included, including 239 males (59.90%) and 160 females (40.10%), with a male-female ratio of 1.49:1.0. There were 349 (87.47%) cases in the mild and moderate group, and 50(12.53%) cases in the severe group. Cases were mainly found from March to October, and there were two epidemic peaks. The average age of onset was 15.49±7.37 days. The common clinical manifestations were cough 391(97.99%), stuffy or runny noses 310(77.69%), interlaryngeal sputum sounds 213(53.38%), shortness of breath 192(48.12%). The most common positive signs were pulmonary sputum sounds (182(45.61%)) and moist rales (142(35.68%). (2) There were significant differences in premature birth, low birth weight, previous hospitalization history, breastfeeding(P＜0.05). (3) The clinical manifestations of the two groups were statistically different in fever, cough days after admission, total cough days, shortness of breath, poor appetite, dyspnea, cyanosis, and mental state (irritability/malaise). Lung moist rales (29(58%) and three depression signs (14(28%) were more common in the severe group, while lung sputum sounds (168) were more common in the mild and moderate group (48.14%). There was no statistical difference in blood routine results between the two groups. (4) Logist regression multivariate analysis was performed for the items with statistical differences in (2) and (3), respectively. The results showed that premature birth （OR=3.717，95% CI：1.257 ~ 10.987）was an independent risk factor for the neonatal RSV ALRTI developing into severe infection, shortness of breath（OR=2.216，95% CI：1.061 ~ 4.629）、cyanosis（OR=3.621，95% CI：1.638 ~ 8.004）and three depression signs（OR=2.688，95% CI：1.077 ~ 6.711）was an early warning factor for the neonatal RSV ALRTI developing into severe infection。Conclusion: The common clinical manifestations of ALRTI caused by RSV in neonates were cough、stuffy or runny noses、interlaryngeal sputum sounds and shortness of breath. The neonatal RSV ALRTI with preterm delivery or shortness of breath or cyanosis or three depression signs are more likely to develop severe infections.

关键字 Neonatal; Respiratory syncytial virus; Acute lower respiratory tract infection; Severity index; Severe infection; Risk factors; Clinical features

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The levels and influencing factors of PT-IgG antibody in children with pertussis

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Objective To investigate the levels and influencing factors of serum pertussis toxin IgG (PT-IgG) antibody in children with pertussis. **Methods** The clinical data of children laboratory-confirmed with pertussis and tested for PT-IgG antibody in Shenzhen Children's Hospital from July 2015 to December 2018 were collected and analyzed retrospectively. **Results** In our study, 871 children aged from 6 days to 11 years with a median of 4(2, 7) months were included, among which, 592(68.0%) cases were less than 6 months and 754(86.6%) cases were less than 1 year old. The median course of disease was 15(11, 20) days. There were 452(51.9%) and 346(39.7%) children who were not vaccinated and vaccinated with at least 1 dose, respectively. In terms of age, the PT-IgG levels of children aged 0-2 months, 3-5 months, 6 months-2 years and ≥3 years were 0.7(0.0, 8.2) IU/mL, 2.3(0.0, 23.0) IU/mL, 24.6(0.0, 112.3) IU/mL and 24.9(0.0, 114.7) IU/mL, respectively. The PT-IgG levels of children after onset of symptoms at 0-2 weeks, >2-4 weeks, >4-8 weeks and >8 weeks were 0.0(0.0, 7.9) IU/mL, 8.7(0.0, 56.0) IU/mL, 26.6(5.1, 82.9) IU/mL and 68.0(15.3, 118.8) IU/mL, respectively. The PT-IgG levels were 0.9(0.0, 12.7) IU/mL and 14.6(0.0, 86.3) IU/mL in children who were unvaccinated and vaccinated with at least one dose, respectively. Their age, course of disease and vaccination status were independent influencing factors of PT-IgG levels (β=0.108, 0.189, 0.250, P=0.002, <0.001, <0.001). Taking PT-IgG≥80 IU/mL as cut-off value, 16.0%(139/871) children met the diagnosis, which were 34.3%(12/35) for children ≥3 years old and 46.2%(6/13) for children ≥3 years old with a disease course >2 weeks. **Conclusions** The levels of PT-IgG antibody in children with pertussis is influenced by age, course of disease and vaccination status. The false negative rate of 80 IU/ml as cut-off value in the diagnosis of pertussis is very high, which may lead to a significant increase of missed diagnosis. Therefore, it is necessary to further explore the standards suitable for children in China.

关键字 pertussis; children; PT-IgG antibody

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Clinical characteristics and antimicrobial resistance analysis in pediatric invasive salmonella infectious disease

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[Objective] To analyze the clinical characteristics and antimicrobial resistance of invasive salmonella infections in children. [Methods] Hospitalized children with culture proven invasive salmonella infections from January 2016 to December 2019 in our hospital were retrospectively collected. Clinical manifestations, laboratory tests, serotypes and antimicrobial susceptibility tests of invasive salmonella isolates were analyzed. [Results] A total of 41 isolates of invasive salmonella, 34 (82.9%) were cultured from blood, 4 from joint effusion, 2 from cerebrospinal fluid, and 1 from bone marrow. The major serotypes were S. enteritis (9 cases, 22.0%) and S. typhimurium (7 cases, 17.1%) . Of the 41 patients, the median age was 17 months (IQR: 11, 25 months), and 30 cases (73.2%) were younger than 2 years old. 11 cases (26.8%) had underlying diseases, 32 cases (78.0%) occurred in summer and autumn (from June to November). 40 cases (97.6%) had fever, 21 cases (51.2%) had diarrhea, 14 cases (34.2%) had cough, and 6 cases (14.6%) had convulsion. There were 11 cases of hepatomegaly and 5 cases of splenomegaly. The proportion of eosinophils decreased in 18 cases (43.9%). The CRP level of children with salmonella septicemia company with diarrhea was higher than that of children without diarrhea (P = 0.009). The resistance rates of 41 salmonella strains to ampicillin and ampicillin/sulbactam were higher than 40%, the resistance rates to ciprofloxacin and ceftriaxone were 28.6% and 14.6% respectively, the resistance rates to cefepime and levofloxacin were both lower than 5.0%. No meropenem resistant strains were detected. [Conclusion] The peak age of children with invasive salmonella infections was younger than 2 years old. Bloodstream was the major site of invasive salmonella disease. The manifestations were various and atypical. It is critical to pay attention to the antimicrobial resistance of salmonella strains in children.

关键字 Salmonella; serotype; resistance; invasive; children

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Clinical characteristics and prognostic factors in children with streptococcus pneumoniae blood-stream Infection : a multicenter clinical study

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Objective To explore the clinical characteristics and prognostic factors of in Chinese children with Streptococcus pneumoniae(Spn) bloodstream infections. Methods The clinical data of 337 children with Spn bloodstream infections admitted from 11 hospitals in China from January 2016 to December 2018 were retrospectively analyzed. Patients were divided into poor prognosis group (n=40) and good prognosis group (n=297) according to the outcome at discharge, risk factors of poor prognosis were analyzed by multivariate Logistic regression analysis. Result Among the 337 cases, there were 209 males and 128 females, 254 cases (75.4%) were under 3 years old, 217 cases(64.4%) occurred in winter and spring, 156 cases (46.3%) were from rural areas. There were 320 cases (95%) of community-acquired infection. Among the 60 (17.8%) cases with underlying diseases, the top 5 included 15 cases (25%) with preterm or low birth weight, 10 cases (16.7%) with history of severe trauma or surgery, 9 cases(15%) with congenital heart disease, 5 cases (8.3%) with acute leukemia and 4 cases (6.7%) underwent hematopoietic stem cell transplantation. The primary symptom of 334 (99.1%) cases was fever, the fever course of 120 cases (35.6%) were more than 7 days. There were 138 cases (40.9%) with pneumonia, 102 cases (30.3%) with sepsis, and 62 cases (18.4%) with bacterial meningitis. 11 cases (3.26%) were coinfected with mycoplasma pneumoniae, 1 case (0.3%) with RSV and 1 case (0.3%) with adenovirus. There were 246 cases (73%) with WBC＞$12*10^9$/L，28 cases (8.3%) with WBC<$4*10^9$/L , 44 cases (13.1%) with PLT<$100*10^9$/L, 26.75%(88/329 cases) with CRP>100mg/L and 41.3%(106/257 cases) with PCT>2ug/L. The drug sensitivity test of 331 Spn strains showed that the insensitivity rate of penicillin was 77.9%, and the multiple resistance rate was 97.9%. There were 40 cases (11.87%) in the poor prognosis group and 297 cases (88.13%) in the good prognosis group. The independent risk factors of poor prognosis were complicated with meningitis(*OR*=4.470、95%*CI*：1.809~11.042、*P*=0.001)、sepsis(*OR*=2.713、95%*CI*：1.115~6.602、*P*=0.028)、shock(*OR*=15.536、95%*CI*：4.731~51.021、*P*=0.000)、WBC＞$12*10^9$/L(*OR*=4.890、95%*CI*：1.137~21.027、*P*= 0.033)、WBC＜$4*10^9$/L(*OR*=13.978、95%*CI*：2.521~77.514、*P*= 0.003)、endotracheal intubation and mechanical ventilation(*OR*=5.557、95%*CI*：2.099~14.716、*P*=0.001). Conclusion Boys under 3 years old and with underlying diseases are more susceptible to Spn bloodstream infection. Pneumonia, sepsis and meningitis are common. The rate of poor prognosis is still high despite active treatment. Meningitis, sepsis, shock, WBC＞$12*10^9$/L，WBC＜$4*10^9$/L, endotracheal intubation and mechanical ventilation are risk factors of poor prognosis.

关键字 Streptococcus pneumoniae bloodstream infection; Clinical characteristics; prognosis; influence factor; Multicenter study

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Peripheral immune profile of children with Talaromyces marneffei infections: A retrospective analysis of 21 cases

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Background Talaromyces marneffei (T. marneffei) is an opportunistic pathogen that infects immunodeficient children. The aim of the study is to determine the clinical features and peripheral immune state of Talaromyces marneffei (T. marneffei) infections in children for early detection and diagnosis.

Methods We retrospectively reviewed 21 pediatric patients who were diagnosed with T. marneffei infections and were followed up in the Guangzhou Women and Children's Medical Center from January 2010 to January 2020. For each patient, we collected and analyzed clinical characteristics, peripheral immunological results, genetic tests, complications and prognosis.

Results Common clinical features of the patients included fever (20/21, 95.24%), cough (17/21, 80.95%) and hepatomegaly (17/21, 80.95%). Severe complications included septic shock (12/21, 57.14%), hemophagocytic lymphohistiocytosis (HLH) (11/21, 52.38%), acute respiratory distress syndrome (ARDS) (10/21, 47.62%), multiple organ dysfunction syndrome (MODS) (9/21, 42.86%), and disseminated intravascular coagulation (DIC) (7/21, 33.33%). Eleven children (11/21, 52.38%) eventually died of T. marneffei infections. All patients were HIV negative. Seven cases revealed reduced antibody levels, especially IgG. Higher levels of IgE were detected in 9 cases with an obvious increase in two patients. Ten patients showed decreased complement C3 levels, some of whom had low C4 levels. Three patients displayed decreased absolute T lymphocyte counts, including the CD 4+ and CD 8+ subsets. A reduction in NK cells was present in most patients. No patient had positive nitro blue tetrazolium (NBT) test results. Nine patients were screened for common genetic mutations.Of the cases, one case had no disease-specific gene mutation. Four children had confirmed hyperimmunoglobulin M syndrome (HIGM) with CD40LG variation, one case had severe combined immunodeficiency (SCID), and one case had hyper-IgE syndrome (HIES). One patient was identified as having a heterozygous mutation in STAT3 gene; however, he showed no typical clinical manifestations of HIES at his age. One patient had a mutated COPA gene with uncertain pathogenic potential. Another patient was diagnosed with HIES that depended on her clinical features and the National Institutes of Health (NIH) scoring system.

Conclusions T. marneffei infections in HIV-negative children induced severe systemic complications and poor prognosis. Children with T. marneffei infections commonly exhibited abnormal immunoglobulin levels in peripheral blood, particularly decreased IgG or increased IgE levels, further suggesting possible underlying PIDs in these patients.

关键字 Talaromyces marneffei, complication, immunity, primary immunodeficiency diseases, children

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Characterization of Pneumocystis jirovecci pneumonia in HIV- and hematologic/oncologic disease-free children: a case series report and literature review

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Background: Guidelines for the diagnosis, prevention and treatment of Pneumocystis jirovecci pneumonia(PJP) are available for children with human immunodeficiency virus(HIV) or hematologic/oncologic diseases, but not for children with other underlying conditions who are the population we focus on in the study.
Case presentation: This case series describes six children with an immunocompromised status or a potential primary immune deficiency (PID), presenting clinical syndromes indicative of PJP. They had a low CD4+ T-cell count and/or ground glass opacities (GGO) in the chest image. None were HIV-positive, suffered from hematologic/oncologic diseases, or were receiving chemoprophylaxis. PJP was confirmed in the six children by Gomori methenamine silver staining and detection of the pathogen’s genome by metagenomic next-generation sequencing (mNGS). PID was ascertained in five of the children upon hospitalization. Five children were administered trimethoprim/sulfamethoxazole (TMP/SMZ) against PJP. One child received combined therapy with TMP/SMZ and micafungi. Five children recovered without pulmonary sequela, while one child deceased.
Conclusions: Once a low CD4+ T-cell count or a GGO in the chest image is observed in an immunocompromised or possible PID child with compatible clinical syndrome of PJP, it is advisable to perform a bronchoscopy with broncho-alveolar lavage and test the presence of the pathogen using smear staining and mNGS. TMP/SMZ remains the first choice treatment, and a combination therapy with TMP/SMZ and micafungi can be considered when necessary. PID must be screened and whole-exome sequencing is preferred.

关键字 Pneumocystis jirovecci pneumonia, diagnosis, case report, primary immune deficiency

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Save An Infant With Out-Of-Hospital Sudden Death Caused By Pertussis

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Background: Although it is recognized that pertussis can cause death in vulnerable infants, out-of-hospital sudden death caused by pertussis is rare and the mechanism is unclear.
Case presentation: A 24-day-old, 5kg, male infant presented cough without fever. On the 12th day of the illness, an unexpected sudden death occurred outside the hospital. After 10 minutes of cardiopulmonary resuscitation, the infant was successfully resuscitated and admitted to Pediatric Intensive Care Unit. Emergency laboratory examination showed hypoglycemia and hyponatremia. His nasopharyngeal swab tested positive for Bordetella pertussis by polymerase chain reaction and culture. After mechanical ventilation, antibiotics and other symptomatic treatments, the infant recovered.
Conclusion: To our knowledge, this is the first report discussing the mechanism of sudden death caused by pertussis. Hypoglycemia, hypoxemia and hyponatremia associated with severe pertussis lead to the sudden death in our case. This will help doctors increase their awareness and vigilance of pertussis as a disease that can cause sudden death.

关键字 infant, sudden death, pertussis

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The clinical features of anti-tuberculosis drug-induced liver injury in Chinese children: a case-control study

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Aim: Liver injury caused by first-line anti-tuberculosis medications is a severe drug adverse effect that causes treatment interruption and unfavorable treatment outcome. The clinical characteristics and factors associated with anti-tuberculosis drug-induced liver injury (AT-DILI) in Chinese pediatric patients remain unclear. This study aimed to investigate the clinical features and factors associated with AT-DILI in Chinese children.
Methods:We retrospectively enrolled children diagnosed with drug-sensitive tuberculosis in Children's Hospital of ChongQing Medical University between 2014 and 2019. Demographic and clinical characteristics were collected via the electronic hospital information system.
Results: Among 746 patients diagnosed with drug-sensitive tuberculosis, 30 patients developed liver injury. The overall incidence of AT-DILI in Chinese children was 4.02%. Most of the AT-DILI cases occurred within one month and presented as a mild process. Most patients (86.67%) presented the hepatocellular injury type. Pyrazinamide and rifampin were the main implied agents. Automatic linear modeling revealed that the liver injury was associated with total bile acid, γ-glutamyltranspeptadase, and lactate dehydrogenase, but not with age, nutrition status, and tuberculosis type. More than half of the patients with AT-DILI recovered within one month after drug withdrawal; moreover, there was no case of acute liver failure during treatment.
Conclusion: Our findings demonstrate that in Chinese children, AT-DILI appeared within one month and presented as a mild process. We recommend regular liver function tests at 2-week intervals during the intensive phase, as well as monitoring of the total bile acid and γ-glutamyltranspeptadase levels in addition to the traditional monitoring of bilirubin and transaminase.

关键字 pediatrics, drug-sensitive tuberculosis, drug-induced liver injury, clinical characters

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Identifying potential biomarkers in hepatitis B virus infection and its response to the antiviral therapy by integrated bioinformatic analysis

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Aim:An integrated bioinformatic analysis was performed to investigate the host factors that affect the therapeutic responsiveness in chronic hepatitis B(CHB) patients.
Methods:Gene expression profiles concerning therapeutic responsiveness in CHB patients were downloaded from Gene Expression Omnibus(GEO) and analyzed to identify differential expressed genes(DEGs). Enrichment analyses of DEGs were conducted using DAVID database. Immune cell infiltration characteristics were analyzed by CIBERSORT. Upstream miRNAs and lncRNAs of hub DEGs were identified by miRWalk 3.0, miRNet in combination of MNDR platform.
Results:4 GEO datasets were chosen and analyzed. 77 overlapped DEGs and 15 hub genes were identified. Enrichment analyses revealed that the DEGs were mainly enriched in immune response and chemokine-signaling. Investigation of immune cell infiltration in liver samples suggested significantly different infiltration between responders and nonresponders, mainly characterized by higher proportions of CD8+ T cells and activated NK cells in nonresponders. Prediction of upstream miRNA and lncRNA detected a potential mRNA-miRNA-lncRNA regulatory network composed of 2 lncRNAs, 5 miRNAs and a targeting mRNA CCL5.
Conclusion: Our study suggested that host genetic factors might affect the therapeutic responsiveness in CHB patients. The antiviral process was associated with chemokine-mediated immune response, immune cell infiltration in liver microenvironment and a potential mRNA-miRNA-lncRNA network targeting chemokine CCL5.

关键字 Chronic hepatitis B; Bioinformatic analysis; Therapeutics; Immune cell infiltration; lncRNA; miRNA

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Fatal pediatric Stevens-Johnson syndrome/toxic epidermal ecrolysis: Three case reports

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Rationale: Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN) are extremely rare but potentially life-threatening disorders. We presented 3 fatal pediatric SJS/TEN cases.
Patient concerns: Our patients had some severe complications such as septic shock, respiratory failure and obliterans bronchiolitis (BO) etc. DIAGNOSIS:: Three patients diagnosed SJS/TEN with clinical symptoms that were triggered by antibiotics, nonsteroidal anti-inflammatory drugs, previous infection, or neoplasms.
Interventions: All of them accepted mechanical ventilation, intravenous immunoglobulin (IVIG), blood transfusion, glucocorticoid, and multi-anti-infectious therapy.
Outcomes: They all died because of out-of-control severe infections. In Patient 1, he died 6 days after being admitted to the PICU on the 28th day from onset. In Patient 2, he died on the 211th day from the onset of illness during the third time of PICU admission. In Patient 3, she died 12 days after PICU admission on the 87th day from onset.
Lessons: We should be aware that mucosal damage occurs on the skin and within the mucosa of visceral organs, leading to the occurrence of bronchiectasia, BO, enterocolitis, acute renal failure, and severe secondary infections. Establish a clinically predictive score that includes severe infection for pediatric patients to evaluate the risk of mortality in children in order to improve poor outcomes.

关键字 Stevens-Johnson syndrome，toxic epidermal ecrolysis，pediatric

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The clinical epidemiological characteristics of pertussis in Children and the prevalence of infection in close contacts

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Objective To investigate the clinical epidemiological characteristics of children with pertussis and the infection of their close family contacts in our hospital.
Methods The clinical data of children with pertussis and the etiological detection results of close family contacts in our hospital from 2015 to 2018 were collected and descriptive epidemiological analysis was carried out.
Results A total of 2716 cases of pertussis in children were reported in our hospital from 2015 to 2018, with 504 cases, 425 cases, 796 cases and 991 cases per year, respectively. The most cases was in May 2015 (72 cases), in August 2016 and 2018 (68 cases in 2016 and 144 cases in 2018), and in July 2017 (115 cases). A total of 1517 boys and 1199 girls were reported in the past 4 years, the ratio of male-to-female is 1.27:1. The proportion of children under 1 year old was 79.71%（2165/2716）, of which 74.36%（1610/2165）was less than 6 months old. Among the reported cases, 1605 (59.09%) were treated as outpatients, aged 5 (3,11) months, and 1111 (40.91%) were hospitalized, aged 4 (2,7) months. There were 876 outpatients (54.41%) and 734 inpatients (45.59%) under 6 months of age, 575 outpatients (63.47%) and 331 inpatients (36.53%) between 6 months and 2 years of age, and 154 outpatients (77.00%) and 46 inpatients (23.00%) with above 2 years old, respectively. There were statistically significant differences among the three groups of children in outpatient and inpatient treatment distribution（c2=48.304，P＜0.001）. The average hospitalization time of inpatients under 6 months of age was （8.45±3.90） days, that of inpatients between 6 months and 2 years of age was （7.14±3.72） days, and that of inpatients above 2 years old was （6.80±3.32） days. There was significant difference in hospitalization days among the three age groups（F=17.09，P＜0.001）.Among the confirmed cases of pertussis reported in our hospital, there was one case of recurrent pertussis whose first onset of pertussis occurred 3 years after completion of four doses of DTaP. The interval between two pertussis episodes in this case was 1.5 years. The etiological test results of pertussis were collected from 617 close family contacts of 270 reported cases, including 249 mothers, 130 grandparents, 146 fathers, 60 brothers and sisters, and 32 others (including uncle, aunt, father's sister, mother's brother, wife of mother's brother, mother's sister, grandaunt, nanny). The number of positive cases and positive rate were 87 (34.94%), 34 (26.15%), 36 (24.66%), 11 (18.33%) and 5 (15.63%), respectively. Mother's positive detection rate is significantly higher than other groups, there were statistically significant differences among the groups（c2=12.178，P=0.016）.
Conclusion In the past 4 years, the number of reported cases of pertussis in our hospital fluctuated and increased year by year, with high incidence in summer and autumn, mainly in children under 1 year old, and more males than females. Outpatient treatment was more than inpatient treatment, and the age was significantly older than inpatient treatment.The younger the children, the higher the rate of hospitalization, and with the increase of the age of hospitalized children, the length of hospitalization was significantly shortened. Pertussis can be reinfected after natural infection, and vaccination don't get lifetime immunity. Among close

family contacts with reported cases of pertussis in children, the mother has the highest rate of infection and may be a main source of pertussis infection in children.

关键字 Pertussis; Epidemic characteristics; Recurrent pertussis ;Close contact

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Establishment and Application of a Multiple Cross Displacement Amplification Coupled With Nanoparticle-Based Lateral Flow Biosensor Assay for Detection of Mycoplasma pneumoniae

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Background: To improve the diagnosis of Mycoplasma pneumoniae infection in children for early effective antimicrobial treatment.
Method: We established a multiple cross displacement amplification (MCDA) coupled with a nanoparticle-based lateral flow biosensor (LFB) assay (MCDA－LFB) for Mycoplasma pneumoniae detection. Then, this assay was applied to 197 oropharyngeal swab samples collected from children highly suspected of M. pneumoniae infection, and compared to culture-based method and real-time PCR assay.
Results: The optimal reaction conditions of MCDA-LFB assay for Mycoplasma pneumoniae detection were found to be 30min at 65◦C and detection results were visually reported using a biosensor within 2min. The Mycoplasma pneumoniae－MCDA－LFB method specifically detected only Mycoplasma pneumoniae templates, and no cross-reactivity was generated from non- Mycoplasma pneumoniae isolates. The analytical sensitivity for this assay was 50 fg of genomic templates in the pure cultures, as obtained from colorimetric indicator and real-time turbidimeter analysis. The detection rates of Mycoplasma pneumoniae using a culture-based method, real-time PCR assay, and MCDA－LFB assay were 8.1% (16), 33.0% (55), and 52.3% (103), respectively, which indicated that the MCDA－LFB assay was superior to the culture-based method and real-time PCR method for detection of target agent. Using this protocol, 25min for rapid template extraction followed by MCDA reaction (30min) combined with LFB detection (2min) resulted in a total assay time of ～60min.
Conclusions: The MCDA－LFB assay established in this report was a simple, rapid, sensitive, and reliable assay to detect Mycoplasma pneumoniae strains, and can be used as a potential diagnostic tool for Mycoplasma pneumoniae in basic and clinical laboratories.

关键字 Keywords: Mycoplasma pneumonia, multiple cross displacement amplification, nanoparticle-based biosensor, lateral flow biosensor, MCDA－LFB

分类：15. Infectious Disease 感染
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Increased macrolide resistance rate of M3562 Mycoplasma pneumoniae correlated with macrolide usage and genotype shifting

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Background: Macrolide-resistant Mycoplasma pneumoniae (MP) strains have been spreading widely in China, causing difficulties in the treatment of Mycoplasma pneumoniae pneumonia (MPP), especially in children. To characterize MP strains and to clarify the continuous high rates of macrolide resistance, 1524 oropharyngeal swabs collected from children in Beijing Children’s Hospital infected with MP during 2016-2019 were analyzed.
Method: Real-time PCR assay was used to confirm the presence of MP and to detect mutations associated with macrolide resistance. Multiple locus variable number tandem repeat analysis (MLVA) was performed to illustrate the epidemiological and molecular characteristics of MP strains. The clinical data was collected from medical records.
Results: Among the 1524 samples, 1386 harbored mutations associated with macrolide resistance; 1049 samples were successfully classified into 11 genotypes. The proportion of the predominant type, M4572, decreased from 84.49 to 70.77% over the time period examined, while that of M3562 increased from 11.63 to 24.67%. Notably, we also found that the frequency of macrolide resistance in M3562 drastically increased, from 60% in 2016 to 93.48% in 2019. Clinical data suggested that the frequency of resistant M3562 was higher in the macrolide usage group than in the nondrug usage group (90.73 vs 53.57%, P=0.000), while the resistance rate of M4572 was not substantially affected by previous macrolide exposure.
Conclusions: These findings validated that antimicrobial application and clonal expansion of resistant MP strains play important roles in the high rates of macrolide resistance.

关键字 Keywords: Mycoplasma pneumoniae, macrolide resistance, genotype, disease severity, pediatrics.

分类：15. Infectious Disease 感染
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Ultrasensitive and specific detection of group B streptococcus using multiple cross displacement amplification-based assays

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Purpose The aim of this study was to provide accurate and rapid diagnosis tests for GBS screening which are beneficial to pregnant women at delivery.
Methods We employed the multiple cross displacement amplification (MCDA) to devise a rapid GBS testing, and three monitoring techniques, including visual detection reagent (VDR), nanoparticle-based lateral flow biosensor (LFB) assay and fluorescent method (EvaGreen), were selected for indicating the MCDA results. A set of MCDA primers was designed according to the cfb gene, which is specific to target pathogen.
Results The optimal temperature for the GBS-MCDA assay was 64℃, and time condition for 30 min. GBS-MCDA could correctly identified 5 strains of GBS, and no positive signals were obtained from 24 non-GBS strains. The assay's sensitivity was 100 fg per reaction in pure culture. The whole process of GBS-MCDA assay, including rapid template extraction (25 min), MCDA reaction (30 min) and results reporting (2 min), could be finished within 60 min. To demonstrate its feasibility, GBS-MCDA assay was used to detect 30 clinical samples, the results were consistent with PCR.
Conclusion These data showed that the GBS-MCDA assays developed here are applicable for the rapid and specific detection of GBS.

关键字 group B streptococcus, multiple cross displacement amplification, visual detection reagent, lateral flow biosensor, EvaGreen.

分类：15. Infectious Disease 感染
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Epidemiology, risk factors and outcomes of bloodstream infection caused by ESKAPEEc pathogens among hospitalized children

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Background: Bloodstream infection (BSI) resulting from ESKAPEEc (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Escherichia coli, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter spp) is relevant to high mortality and economic cost. Data concerning the impact of BSI due to ESKAPEEc in pediatric population was virtually scant. Our purpose was to summarize the epidemiology, risk factors and outcomes of ESKAPEEc BSI among hospitalized children.
Methods: Inpatients diagnosed with BSI with definite etiology between January 2016 and December 2018 were enrolled retrospectively at the West China Second University Hospital. Data were systematically reviewed on patient' clinical characteristics and laboratory findings to ascertain independent predictors, clinical features and outcomes.
Results: Of the 228 patients with BSI, 174 (76.3%) were caused by ESKAPEEc (124 MDR-ESKAPEEc). Multivariate analysis demonstrated that premature and/ or low birth weight (odds ratio [OR] = 2.981, P= 0.036), previous surgery and/or trauma (OR=5.71, P=0.029) and source of urinary tract infection (OR=10.6, P=0.004) were independently associated with ESKAPEEc BSI. The independent risk factor for MDR-ESKAPEEc BSI was nosocomial infection (OR=3.314, P=0.037). The overall mortality rate in patients with ESKAPEEc BSI was 14.4% (25/174), and no significant difference was ascertained in mortality between MDR-ESKAPEEc and non-MDR ESKAPEEc BSI groups (13.7% vs. 11.4%, P=0.692). In addition, previous surgery and/or trauma, thrombocytopenia, mechanical ventilation were significant risk factors for mortality caused by ESKAPEEc BSI.
Conclusions: More than two-thirds of BSI among hospitalized children were caused by ESKAPEEc. Previous surgery and/or trauma, thrombocytopenia and mechanical ventilation increased the risk rate for mortality in ESKAPEEc BSI. The risk factors ascertained could assist physicians to early suspect ESKAPEEc and MDR ESKAPEEc.

关键字 ESKAPEEc pathogens, bloodstream infection, children

分类：15. Infectious Disease 感染
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Screening of latent tuberculosis infection in hospitalized children

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Abstract
OBJECTIVE: This study aimed to identify a screening strategy appropriate to the Chinese context in latent tuberculosis infection (LTBI) children with different exposure levels, and explore the clinical significance of discordant results.
METHODS: We enrolled hospitalized children with respiratory infectious diseases (RID) for LTBI screening using tuberculin skin test (TST) and interferon-g release assay (IGRA) T-SPOT.TB during 2013-2015. Participants were classified into three subgroups according to their exposure level with TB (i.e. without reported contact risk, with household risk, and with non-household risk).
RESULTS: Finally, 6202 children (median age: 4.76 years; interquartile range: 1.0-8.0 years) were enrolled. Children with no contact history had the lowest positive percentages of IGRA (0.7%) and TST (3.3%). As the exposure level increased, the positivity of the two tests proportionally increased accordingly. The positive percentage of TST was much higher than that of IGRA in all of the three groups. Exposure level is significantly associated with IGRA+/TST+ results. Children with IGRA+/TST+ results had larger mean value of indurations than those with IGRA-/TST+ results (15mm vs 13mm, P=0.02). They also showed significantly higher numbers of IFN-γ secreted T cells responded to early-secreted antigenic target 6-kDa protein (45.6±70.0 vs 11.0±12.5, p=0.015) and culture filtrate protein 10 (31.9±45.6 vs 11.8±9.7, p=0.03)than those with IGRA+/TST- results .
CONCLUSIONS: Both IGRA and TST showed increased positivity among children along with the increasing of exposure level.

关键字 latent tuberculosis infection; screen, TST, IGRA

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A 3-week case review of outpatient children from epidemic area

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【Abstract】Objective Retrospective analysis was performed on 57 cases of children treated in tongji hospital affiliated to tongji medical college of university of science and technology in recent 3 weeks. Method 57 cases were selected from 2020-2-2 to 2020-2-23 and divided into 3 groups, namely the confirmed case group, the suspected case group and the monitoring case group. General data, epidemiological history, clinical manifestations, laboratory examination, imaging data and treatment outcome of each group were collected for analysis. Result There were 11 cases in the confirmed case group (19.3%), including 10 cases (91%) with family cluster history, 7 cases (63.6%) with fever, 2 cases (18.2%) with early peripheral blood leukopenia, 0 case (0.0%) with lymphocytopenia and increased platelets, 2 cases (18.2%) with increased CRP, and 10 cases (90.9%) with abnormal CT changes, and all patients in this group were admitted to the isolation ward. In the suspected case group, there were 23 patients (40.4%), 15 cases (65.0%) with family cluster history, 18 cases (78.3%) with fever, 2 cases (8.7%) with patients were transferred to the confirmed cases and were admitted to isolation ward, and the rest were isolated at home, with a good prognosis. There were 23 cases in the monitoring group (40.4%), among which 4 cases (17.4%) had family cluster history, 13 cases (56.5%) had fever, 9 cases (39.1%) had abnormal CT changes,4 cases (17.4%) were suspected,9 cases (43.5%) were admitted to the general ward,1 cases (4.3%) to the intensive care unit, and 9 cases (39.1%) were treated at home after exclusion of new crown infection, with a good prognosis Conclusion Children with 2019 novel coronavirus infection were mainly characterized by closely family contact, and there was no specificity in clinical manifestations and laboratory examination. Imaging examination had certain guiding significance in the diagnosis and treatment outcome of coronavirus. Strict screening can help to control the spread of 2019 novel coronavirus infection and reduce the risk of nosocomial infection.

关键字 2019 novel coronavirus; Epidemic area; Children; Analysis

分类：15. Infectious Disease 感染
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Clinical characteristics and efficacies of antiviral agents in hospitalized children with infectious mononucleosis in China: A multicenter retrospective study

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Importance: The clinical characteristics of infectious mononucleosis (IM) in Chinese children have not been evaluated in multicenter studies, and the efficacies of antiviral treatment are controversial.
Objective: To investigate the clinical characteristics of Chinese children with IM and current status of antiviral therapy for affected patients.
Methods:Hospitalized patients with IMwere enrolled between 2018 and 2020 in five children’s hospitals in China.The clinical characteristics were comparedamong four age groups: <3 years, 3–6 years, 6–10 years, and>10 years.The clinical characteristicsof IM and efficaciesof antiviral therapy were compared among patients receivingacyclovir (ACV), ganciclovir (GCV), and no antiviral therapy (i.e., non-antiviral group).
Results: In total, 499 patients were analyzed; most patients were 3–6 years of age. The most common symptoms and signs included fever (100%), lymphadenopathy (98.6%), pharyngitis (86.4%), eyelid edema (76.8%), and snoring (72.9%). There were significant differences in rash, hepatomegaly, and liver dysfunction among the four age groups. Patients aged <3 years had a lower incidence of liver dysfunction and a higher incidence of rash. Among the 499 patients, 50.1% were treated with GCV, 26.3% were treated with ACV, and 23.6% received no antiviral therapy. Compared with the non-antiviral group, patients in the ACV and GCV groups had longer durations of fever ($P<0.001$). There were no significant differences in the incidences of complications among the three treatment groups.
Interpretation:The incidence of IM in Chinese children peaked at 3–6 years of age. Clinical features of IM varied according to age. Patients receiving antiviral therapy exhibited more serious clinical manifestations than did patients without antiviral therapy. The efficacy of antiviral therapy for IM requires further analysis.

关键字 Infectious mononucleosis, Antiviral, Ganciclovir, Acyclovir

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The Socio-economic impacts of COVID-19 pandemic in Taiwan

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Abstract Content The infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV 2) resulted in coronavirus disease 2019 (COVID-19). The pandemic of COVID-19 often resulted in a lockdown and had significant socio-economic impacts in the world. This study aimed to elucidate the socio-economic impacts of COVID-19 pandemic in Taiwan.

Methods We retrospectively analyzed the public data collected from the Taiwan centers for disease control (Taiwan CDC), the National Health Insurance (NHI) Administration Ministry of Health and Welfare of Taiwan, and the National Statistics of Taiwan. The package STATA 14 software was applied for the statistical analysis of this study, and a P-value < 0.05 was regarded as statistically significant in this analysis.

Results Since the Dec 2019 to Jun 2021, total 14,005 COVID-19 patients were confirmed in Taiwan. The seasonal case number of COVID-19 is positively correlated with the consumer price index (CPI) (correlation coefficient = 0.71, P = 0.04) in this time period. The case number is not correlated with the overall mortality rate due to any cause (P = 1.00), crude birth rate (P = 0.34), gross domestic product (GDP) (P = 0.32), gross national income (GNI) (P = 0.36) and personal average income (P = 0.36). The seasonal COVID-19 mortality is also positively correlated with CPI (correlation coefficient = 0.72, P = 0.04) during this period.

Conclusion The CPI is an important indicator of inflation, and both the seasonal COVID-19 case number and COVID-19 mortality rate were correlated with CPI in this analysis. The COVID-19 pandemic does not correlate with mortality due to other causes and the crude birth rate in Taiwan.

Key words COVID-19, consumer price index, gross domestic product

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分类：15. Infectious Disease 感染
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Primary Ciliary Dyskinesia combined with Mycobacterium avium: A case report and literature review

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Primary ciliary dyskinesia (PCD), including immobile cilia syndrome, Kartagener syndrome, cilia dyskinesia and primary ciliary disorientation immobile cilia syndrome, is an autosomal recessive disorder resulting from loss of normal ciliary function. Kartagener syndrome is characterized by the combination of PCD and situs inversus, and occurs in approximately half of patients with ciliary dyskinesia. Abnormal function of the respiratory tract cilia is common, causing repeated respiratory infections. Non-tuberculous mycobacterial disease refers to infection with non-tuberculous mycobacteria (NTM) and lesions of related tissues and organs. Accumulating evidence has revealed that patients with underlying lung diseases (bronchiectasis, chronic obstructive pulmonary disease, cystic fibrosis, PCD, allergic bronchopulmonary aspergillosis, etc.) are susceptible to NTM lung diseases. Herein, we reported a 16-year-old girl who was diagnosed with PCD through sinus CT, chest high-resolution CT (HRCT) and whole exome sequencing (WES) due to repeated coughing and expectoration for more than eight years. She referred to our unit for fever, cough and expectoration for half a month. The acid-fast stain of bronchoalveolar lavage fluid (BALF) was positive, and metagenomic next generation sequencing (mNGS) of BALF showed Mycobacterium avium (M. avium). Azithromycin, rifampicin, ethambutol, and linezolid were administered regularly. Coughing decreased on the 12th day of admission, and blood oxygen saturation was maintained at a normal level. On the 16th day, the body temperature was mainly low fever, and the heat peak remained below 38° C. She was discharged home.

关键字 Primary ciliary dyskinesia, Kartagener syndrome, Mycobacterium avium, metagenomic next generation sequencing, ethambutol, imipenem, linezolid

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linical Features and Risk Factors Analysis of Bronchitis Obliterans due to Refractory Mycoplasma Pneumoniae Pneumonia in Children: A Nomogram Prediction Model

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Background
Early prediction of bronchitis obliterans (BO) is of great significance to the improvement of the long-term prognosis of children caused by refractory mycoplasma pneumoniae pneumonia (RMPP). This study aimed to establish a nomogram model to predict the risk of BO in children due to RMPP.
Methods
A retrospective observation was conducted to study the clinical data of children with RMPP (1-14 years old) during acute infection. According to whether there is BO observed in the bronchoscope, children were divided into BO and the non-BO groups. The multivariate logistic regression model was used to construct the nomogram model.
Results
141 children with RMPP were finally included, of which 65 (46.0%) children with RMPP were complicated by BO. According to the multivariate logistic regression analysis, WBC count, ALB level, consolidation range exceeding 2/3 of lung lobes, timing of macrolides, glucocorticoids or fiber bronchoscopy and plastic bronchitis were independent influencing factors for the occurrence of BO and were incorporated into the nomogram. The area under the receiver operating characteristic curve (AUC-ROC) value of nomogram was 0.899 (95% confidence interval [CI]: 0.848~0.950). The Hosmer-Lemeshow test showed good calibration of the nomogram (p=0.692).
Conclusion: A nomogram model found by seven risk factor was successfully constructed and can use to early prediction of children with BO due to RMPP.

关键字 Refractory Mycoplasma Pneumoniae Pneumonia; Bronchitis Obliterans; Fiberoptic Bronchoscopy; Nomogram Model; Prediction

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Emergence of Klebsiella pneumoniae ST307 and Escherichia coli ST131 Co-Producing CTX-M with SHV and KPC from Paediatric Patients at Shenzhen Children's Hospital, China

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Abstract Content The rise and spread of antimicrobial resistant bacteria are universal symbolic challenges for healthcare due to the restricted treatment choices. In the past year, carbapenem resistant *Klebsiella pneumoniae* (CRKP) and extended-spectrum β-lactamases (ESBLs) *Escherichia coli* infections have become a growing global public health concern, particularly in paediatric patients, due to high morbidity and mortality. We investigated the clonal diversity of carbapenemase-producing Klebsiella pneumoniae ST307 and emergence of (ESBLs) particularly CTX-M producing multi-drug-resistant (MDR) Escherichia coli ST131(E. coli) isolates from the Shenzhen Children's Hospital, China. Additionally, drew conclusions on the clinical and public health impact of these isolates as MDR.

Methods From January 2014 to December 2018, a total number of 36 unique carbapenemase-producing clinical isolates of *Klebsiella pneumoniae* were collected out of 900 clinical isolates. A total of 2,670 isolates of *E. coli* were collected from Shenzhen Children's Hospital, China of which 950 were ESBLs producers. ESBLs production was confirmed by using the combination disc diffusion method and carbapenemase-production by using the carbapenem inactivation method (CIM). After carbapenemase/ ESBLs production confirmation, antimicrobial susceptibility, resistance determinants, gene location, plasmid replicon types and phylogenetic relationship were determined.

Results Both isolates showed resistance to ceftazidime, ertapenem, ampicillin, cefazolin, ceftriaxone, cefotetan, ticarcillin, cefaclor, cefpodoxime, azlocillin, cefcapene, mezlocillin and ampicillin-sulbactam. Of the 36 Klebsiella pneumoniae carbapenemase genes coding isolates, bla_{NDM} was the mostly detected 50% (n=18) followed by bla_{KPC} and bla_{IMP} 19% (n=7), bla_{VIM} 17% (n=6), $bla_{OXA-48-like}$ 8% (n=3) and bla_{SME} 5% (n=2), whereas extended-spectrum β-lactamase (bla_{SHV}) was predominantly detected 92% (n=33) followed by bla_{CTX-M} 53% (n=19) and bla_{CMY} 28% (n=10). Pulsed-field gel electrophoresis typing showed eight different patterns, and twenty-five distinct sequences types were observed with ST307 being predominantly identified 11% (n=4), followed by ST2407 8% (n=3). Plasmid replicon typing results indicated that IncFIS, IncHI2, IncFIC and IncFIA plasmids carry bla_{CTX-M}, bla_{SHV} and bla_{NDM} genes. In the case of *E. coli*, 35% (n=950) prevalence of ESBLs-production were reported of which 50 ESBLs producing *E. coli* were randomly selected for a further characterization. All 50 ESBLs producers harboured at least one type of β-lactamase gene particular bla_{CTX-M}. The PCR and sequencing revealed the most common CTX-M subtype was $bla_{CTX-M-15}$ (n=18), followed by $bla_{CTX-M-14}$ (n=16), $bla_{CTX-M-90}$ (n=9), $bla_{CTX-M-55}$ (n=3), $bla_{CTX-M-27}$, $bla_{CTX-M-101}$, and $bla_{CTX-M-211}$ each (n=1). The co-existence of bla_{CTX-M} with bla_{TEM}, bla_{SHV}, bla_{GES}, and bla_{VEB} was detected in few isolates. Among identified sequence types, ST131 (12%) was more dominant in ESBLs-producing E. coli.

Phylogenetic group A was the most prominent group among the ESBLs-producing E. coli based on multiplex PCR.

Conclusion This study reports on the occurrence and spread of carbapenemase and extended-spectrum β-lactamase encoding genes co-existence in sporadic Klebsiella pneumoniae ST307 and Escherichia coli ST131 in paediatric patients from the Shenzhen Children's Hospital, China. We highlight the importance to monitor the emergence and trends of ESBLs-producing isolates in a pediatric healthcare setting. our study stresses on the necessity of long-term monitoring on ESBLs-producing E. coli and carbapenemase producing Klebsiella pneumoniae in hospital environments, especially in Children Hospitals. National programs devoted to the health of children in China need to consider the emerging threat of ESBLs-producing bacteria, and research efforts should be devoted to focus on the molecular characterization of ESBL/ carbapenemase types as well as additional controlled studies assessing risk factors and possible outcomes for children.

Key words Klebsiella pneumoniae, E. coli, carbapenemase, ESBLs, antimicrobial susceptibility, molecular characterization

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分类：15. Infectious Disease 感染
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Cord Blood Biomarkers for Diagnosing Early-Onset Neonatal Sepsis: A Literature Review

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Neonatal sepsis (NS) is a life-threatening disease of organ dysfunction and is associated with high mortality and morbidity rates. Early-onset neonatal sepsis (EOS) occurs within 3 days after birth. EOS is commonly related to intrapartum or intrauterine infection and could be fetal if not treated expeditiously. Early detection is of critical importance in guiding administration of antibiotics and improving prognosis. Although blood isolation of pathogens from normally sterile body fluid or compartment remains the gold standard for diagnosing sepsis, results from cultures are not usually timely for management of neonatal sepsis. More than 200 biomarkers of sepsis, such as C-reactive protein (CRP), procalcitonin (PCT), have been reported in this peripheral blood. These biomarkers are not accurate enough for clinical utility because their specificity, sensitivity and predictive values are variable. Thus, some researchers are targeting cord blood biomarkers. As the cord serves as a vital connection between the mother and fetus, it can reflect the fetal infection at early stage. Several biomarkers in cord blood, including acute phase reactants, cytokine, CD markers and vasoactive agents, may be a promising tool for the detection of neonatal infections. This review collates recent research reports suggest biomarkers in cord blood could be important adjuncts to microbial cultures for the early detection of EOS.

关键字 Early-onset sepsis; Cord blood; Fetal mortality; Biomarkers

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Clinical characters of human adenoviruse type 3 and 7 in hospitalized children with acute respiratory infection in Beijing

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Objective To compare the clinical characters of different type HAdV infection in hospitalized children with acute respiratory infection in Beijing. Methods The respiratory tract specimens collected from hospitalized children with acute respiratory infection from November 2017 to October 2019 in Affiliated Children's Hospital, Capital Institute of Pediatrics were screened for HAdV by direct immunofluorescence (DFA) and/or nucleic acid detection. Then the Penton base, Hexon and Fiber gene of HAdV were amplified from HAdV positive specimens to confirm their HAdV types by phylogenetic tree construction. Clinical data were analyzed for children with predominate type HAdV infection using SPSS 23.0 software. Results There were 392 cases (4.34%, 392/9022) positive for HAdV among 9022 hospitalized children with acute respiratory infection, distributed in all seasons of each year with a peak in winter (from December to February), and another one in August and September. Among these 205 children with confirmed types of HAdV infection, 102 (49.76%, 102 / 205) were positive for HAdV-3 and 86 (41.95%, 86/205) , HAdV-7, respectively, whilst 17 cases were confirmed as HAdV-1，2，4，6，14 or 21.In comparison of clinical characters between the predominate HAdV type 7 and 3 infection, significant differences were shown in ratios of children with wheezing (10 cases vs. 25 cases) （χ^2=5.110, P = 0.024), leukocytosis (WBC>15 ×109/L) (2 cases vs. 10 cases) （χ^2=4.438, P = 0.035), leucopenia (WBC<5×109/L) (25 cases vs. 6 cases)（χ^2=11.156 , P =0.001), procalcitonin level (PCT) >0.5 ng/ml (36 cases vs. 18 cases)（χ^2=11.165, P = 0.002), multilobar infiltration (45 cases vs. 38 cases)（χ^2=4.293, P = 0.038), pleural effusion (23 cases vs. 10 cases)（χ^2=9.252, P=0.002）, severe adenovirus pneumonia (7 cases vs. 2 cases)（χ^2 = 3.908, P = 0.048), and median length of hospital stay (8d (IQR 11-15d) vs. 7d (IQR 5-13d)) (Z= 3.728, P = 0.000). Conclusions HAdV-3 and 7 were the predominate types of HAdV infection in hospitalized children with acute respiratory tract infection in Beijing. Compared with HAdV-3 infection, HAdV-7 infection caused more obvious inflammatory reaction, more severe pulmonary symptoms, longer length of hospital stay, suggesting the clinical necessity of further typing of HAdVs.

关键字 Children; Acute Respiratory Infections; Human Adenoviruses; Types; Clinical characters

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Clinical characteristics and antibiotic resistance profile of invasive MRSA infections in newborn inpatients: A retrospective multicenter study from China

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Abstract

Objective. This study aimed to analyze the clinical characteristics and antibiotic resistance profiles of invasive MRSA infections and determine risk factors associated with invasive MRSA infections in newborn inpatients.

Methods. This multicenter retrospective study of inpatients from eleven hospitals in the Infectious Diseases Surveillance of Pediatrics (ISPED) group of China was performed over a two-year period (2018–2019).

Results. A total 220 patients were included. Among included cases, 67 (30.45%) were invasive MRSA infections, including two deaths (2.99%), while 153 (69.55%) were noninvasive infections. The invasive infections of MRSA occurred at a median age of 8 days on admission, which was significantly younger compared to 19 days in noninvasive cases. Sepsis (86.6%) was the most common invasive infection, followed by pneumonia (7.4%), bone and joint infections (3.0%), central nervous system infection (1.5%), and peritonitis (1.5%). Congenital heart disease, low birth weight infant (<2500g), but not preterm neonates, and bronchopulmonary dysplasia, were more commonly found in invasive MRSA infections. All these isolates were susceptible to vancomycin and linezolid and were resistant to penicillin. Additionally, 69.37% were resistant to erythromycin, 57.66% to clindamycin, 7.04% to levofloxacin, 4.62% to sulfamethoxazole-trimethoprim, 4.29% to minocycline, 1.33% to gentamicin, and 3.13% were intermediate to rifampin.

Conclusions. Low age at admission (≤8 days), congenital heart disease, and low birth weight were associated with invasive MRSA infections in neonates, and no isolates resistant to vancomycin and linezolid were found. Determining these risks in suspected neonates may help identify patients with imminent invasive infections who may require intensive monitoring and therapy.

关键字 Methicillin-resistant Staphylococcus aureus, Invasive infection, Clinical characteristics, Antibiotic resistance, Neonates

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Severe cerebral Malassezia globosa infection due to card 9 deficiency

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Background：As receptors of the innate immune system, pattern recognition receptors (PRRs) are important in interaction with pathogens. As a member of PRRs, Caspase Recruitment Domain-containing protein 9 (CARD9) is an intracellular adaptor protein, which plays an important role in fungal defense. CARD9 deficiency may induce a rare primary immunodeficiency (PID) characterized by central nervous fungal infections.
Case presentation：We report a 13 years old male with a homozygous mutation in CARD9 (NM_052813:exon3:c.263delC), who presented with severe cerebral Malassezia globosa （M.globosa ）infection of the central nervous system.
Conclusion: M.globosa may also cause cerebral infection, particularly in patients with acquired or inborn immunodeficiency. CARD9 deficiency should not be neglected in patients with fungal CNS infection and radiological manifestations compatible with systematic fungal infection.

关键字 CARD9, Malassezia globosa, Cerebral infection, Immunodeficiency

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Clinical characteristics of mycoplasma pneumonia complicated with pulmonary embolism in children

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Objective: To investigate the clinical manifestations and characteristics of examination results of children with mycoplasma pneumoniae (MP) pneumonia complicated with pulmonary embolism.

Methods: The clinical manifestations, laboratory examination results and imaging characteristics of 5 children with MP pneumonia confirmed by CT pulmonary angiography and pulmonary embolism were retrospectively analyzed.

Results: Respiratory symptoms were the main symptoms in the early stage of the disease in 5 children, and chest pain in 3 cases, shortness of breath in 1 case and groin pain in 1 case were found in the later stage.The d-dimer level of blood was significantly elevated in laboratory tests.Imaging showed 3 cases of right pulmonary artery embolism and 2 cases of left pulmonary artery embolism.4 patients were treated with anticoagulant therapy and 1 patient was treated with thrombolytic therapy.

Conclusion: MP pneumonia in children with pulmonary embolism is an immune reaction caused by mycoplasma infection, with low incidence and variable clinical characteristics.Pulmonary embolism should be highly vigilant when accompanied by increased blood D-dimer, which can be clearly diagnosed by CT pulmonary angiography.Anticoagulant or thrombolytic therapy may be selected according to different conditions.

关键字 Children, Mycoplasma, Pulmonary embolism,

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Different treatments for children with clostridium difficile infection: a retrospective study in a pediatric hospital from China

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Objectives: Clostridium difficile infection (CDI) is one of the most common cause in children with antibiotic-associated diarrhea. Fecal microbiota transplantation (FMT) is successfully used to treat CDI. This study aims to evaluate the clinical efficacy of different options.
Methods: A retrospective cohort study of pediatric patients under 18 years old treated for CDI in China from September, 2014, to September, 2020 was performed. Patients were assigned as initial CDI and RCDI. 10-14 days of oral metronidazole (7.5mg/kg, 3 or 4 times daily, n=68) or vancomycin (10mg/kg, 4 times daily, n=41) were given as the therapy for children with an initial episode of CDI. For RCDI, 10-14 days of oral vancomycin (10mg/kg, 4 times daily, n=23) or FMT(n=29) was used.
Results: Of all 109 patients, 58 were boys (53.2%). The median age of these children was 5 years (range, 2-9 years). For the primary therapy, 68 received metronidazole, and 41 received vancomycin. RCDI occurred in 48.53% (33/68) of those initially treated with metronidazole compared with 46.33% (19/41) of those initially treated with vancomycin (P=0.825). The total resolution rate of FMT was 96.6%. There were no SAEs reported after FMT within 24 hours and after 2 months. Four children (4/56, 5.4%) were reported with mild and self-limited AEs. The laboratory findings showed that the CRP and albumin were different(P=0.048). The cure rate of FMT was much higher than the cure rate of antibiotics (96.6% vs 47.8%, P<0.001) for RCDI. For RCDI, we compared costs and of FMT and vancomycin, as well as the length of stays. There was no significant difference between these two groups.
Conclusions: FMT is superior to vancomycin in pediatric RCDI and there was no significant increase in the economic burden. Metronidazole may be used as primary treatment for nonrecurrent CDI in children.

关键字 Clostridium difficile, antibiotic, fecal microbiota transplantation, vancomycin, children

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Therapeutic Effect and Safety Analysis of Linezolid with Different Dosage in the Treatment of Drug-resistant Tuberculosis in Chinese Children

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Background: Linezolid (LZD) has been listed as the group A anti-tuberculosis medicine in drug-resistant tuberculosis. However, the dosage and course of LZD in drug-resistant TB was still controversial in children. In this study, we aimed to evaluate the effectiveness and safety of LZD with different dosage in treating drug-resistance TB in Chinese children.

Method：Patients diagnosed as drug-resistant tuberculosis during Sep, 2016 to Mar. 2021 were enrolled in this study and continuously followed up till the end of anti-TB therapy. Patients were assigned as case group (LZD 10mg/kg twice daily) and control group (10mg/kg once daily). Data including demographic information, therapeutic effects of the first 3 month and the rate of adverse drug reaction (ADR) were collected and analyzed. The Reg No. was ChiCTR2100042287.

Result: A total of 26 children underwent our research with 7 patients in case group and 19 cases in control group. The median age is 6.42 year-old (0.65, 12.31) .The ratio of male to female was 1:1.6. There was no statistical differences in gender, age of onset, location of tuberculosis and severity of TB infection between the two groups. The overall Improvement rate of LZD-based regimen after 3 month was 80.77% (21/26) including 6 cases in the case group and 15 cases in the control group. In detail, four patients (4/7) in the case group and fourteen patients (14/19) in the control group had the improvement of imaging and laboratory result; three patients (3/7) in case group and nine case (9/19) in control group experienced symptomatic improvement; five patients underwent etiological conversion with two patients (2/7) in case group and the other three cases (3/19) in control group respectively. There was no statistical differences in these aforementioned clinical effective rates between the two groups ($P>0.05$). As to the ADR of LZD, a total of fifteen children (57.69%) had adverse drug reaction possibly or probably related to LZD, consisting of six patients (6/7, 85.71%) in the case group and nine (9/19, 47.37%) in the control group. The most common ADRs are hyperlactatemia (12/26, 46.15%) 、anemia (6/26, 23.08%) and granulocytopenia (4/26,15.38%). The incidence of hyperlactatemia in case group was significantly higher than that in control group($P<0.05$).

Conclusion: The effectiveness of the LZD based regimen in treating drug-resistant TB in Chinese children is 80.77% in the first three month. Different dosage of LZD daily has similar clinical effect in Chinese children. However, higher dose LZD seems increase the risk of adverse effect of LZD. In future, enlarged cohort of multi-site study combined with pharmacodynamics and pharmacokinetics is necessary.

关键字 drug-resistant tuberculosis; Linezolid

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Limited value of inflammatory markers in detecting bacterial coinfection and guiding antibiotic use among children with enterovirus infection

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ABSTRACT
Introduction: High levels of inflammatory markers including procalcitonin (PCT), C-reactive protein (CRP), white blood cell (WBC), and percentage of neutrophils (%N) have been observed and considered as evidence of possible bacterial coinfection in children with enterovirus infection, which could result in a high antibiotic prescribing rate. This study aimed to explore the value of PCT, CRP, WBC, and %N in detecting bacterial coinfection and guiding antibiotic use among children with enterovirus infection.
Methods: We did a case-control study of hospitalized children with enterovirus infection. Cases were children with enteroviral and bacterial coinfection. Two controls with single enterovirus infection were matched to each case by age and sex. PCT level, CRP level, WBC level, and %N were compared between cases and controls. Clinical features were also compared in controls with and without antibiotic treatment.
Results: We identified 45 cases and 90 controls. PCT level (median: 0.21 vs. 0.10 ng/mL), CRP level (median: 24.90 vs. 24.1 mg/L), WBC level (median: 15.01 vs. 15.64 ×109/L), and %N (median: 64.70% vs. 67.95%) were not significantly higher in the cases than in the controls ($p < 0.05$). Of the 90 controls, 49 (54%) were prescribed antibiotics. Antibiotic treatment did not significantly shorten the duration of fever or length of hospitalization in the controls.
Conclusion: The value of PCT, CRP, WBC, and %N in detecting bacterial coinfection and guiding antibiotic use among children with enterovirus infection is limited.

关键字 Enterovirus; Procalcitonin; C-reactive protein; Leukocytes; Anti-bacterial agents

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Comparative genomics and phylogenetic analysis of Streptococcus pneumoniae strains: penicillin non-susceptible multidrug resistant serotype 19A isolates

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Streptococcus pneumoniae can cause several diseases including otitis media, sinusitis, pneumonia, sepsis and meningitis. The introduction of pneumococcal vaccines has changed the molecular epidemiological and antibiotic resistance profiles of related diseases. Analysis of molecular patterns and genome sequences of clinical strains may facilitate the identification of novel drug resistance mechanism. Three multidrug resistance 19A isolates were verified, serotyped and the complete genomes were sequenced combining the Pacific Biosciences and the Illumina Miseq platform. Genomic annotation revealed that similar central networks were found in the clinical isolates, and Mauve alignments indicated high similarity between different strains. The pan-genome analysis showed the shared and unique cluster in the strains. Phylogenic analysis showed a close evolutionary relationship between the isolates and *S. pneumoniae* 19F. Mobile elements were predicted in the isolates including prophages and CRISPER systems, which may participate in the virulence and antibiotic resistance of the strains. The presence of 31 virulence factor genes was predicted from other pathogens for PRSP 19339 and 19343, while 30 for PRSP 19087. Meanwhile, 33 genes antibiotic resistance genes were predicted including antibiotic resistance genes, antibiotic target genes and antibiotic biosynthesis gene. Further analysis of the antibiotic resistance genes revealed new mutations in the isolates. By comparative genomic analysis, we contributed to the understanding of resistance mechanism and phylogenetic relationship of the clinical isolates with other serotype strains, which could facilitate the concrete drug resistance mechanism study.

关键字 Streptococcus pneumoniae, antibiotic resistance, penicillin non-susceptible, serotype 19A, genomic analysis, multidrug resistant

分类：15. Infectious Disease 感染
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Global transcriptome analysis of the responses of penicillin resistant Streptococcus pneumoniae clinical isolates to penicillin

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Background: *Streptococcus pneumoniae* is a Gram-positive opportunistic pathogen that colonizes the upper respiratory tract mucosal surface with higher carriage rate in children which could cause otitis media, sinusitis, pneumonia, sepsis and meningitis. Antibiotics were the main treatments for bacterial infectious diseases, while emergence of resistant strains seriously affects clinical therapy. Penicillin resistant pneumococci was on the list of 12 antibiotic resistant priority pathogens that posed major health threat to human distributed by WHO in 2017. It awaits further research to reveal the resistance mechanism for the clinical isolated penicillin non-susceptible strains.
Methods: In this study, pneumococcal isolates were collected, serotyped using multiplex PCR and the antibiotic susceptibility testing was performed according to Clinical and Laboratory Standards Institute (CLSI) methods. Penicillin was added to the culture in the mid-exponential growth phase to final concentrations of 4 μg/ml (1/2 MIC), the bacteria were collected 20 minutes later and used for total RNA extraction. RNA-seq was applied to analyze the differential expression of the genes and sRNA, and RT-qPCR was utilized to verify the results.
Results: The penicillin resistant *Streptococcus pneumoniae* clinical isolates were isolated from the BAFL of a child and identified belonging to the serotype 19A. Amino acid substitutions in the critical motif of penicillin binding proteins (PBPs), PBP2x, PBP2b, and PBP1a were identified for both the penicillin resistant and susceptible clinical isolates. Hence, these isolates were cultivated and stimulated to screen the penicillin resistant related genes by RNA-seq. A total of 119 genes had changed transcription levels with 54 down-regulated and 65 up-regulated expression ($|log2FoldChange| \geq 1$, $padj < 0.05$). The differential expression genes in response to penicillin stress included genes involved in a broad range of cellular processes such as metabolic pathways, phosphotransferase, peptidoglycan biosynthesis, beta-lactam resistance, ABC transporters and sRNA. The differential expression genes were verified using RT-qPCR. The target genes for the sRNA was predicted using the CopraRNA and the predicted genes with opposite changes to the sRNA were focused to verify the concentrate mechanism in the antibiotic resistance.
Conclusion: The genes and sRNA regulated by penicillin stimulation were identified through transcriptome analysis of the PBP mutated penicillin sensitive and resistant clinical strains, which could facilitate further study of the new resistance mechanism.

关键字 Streptococcus pneumoniae，penicillin non-susceptible clinical strains，RNA-seq，resistance mechanism

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Analysis of tuberculin skin test of 3865 healthy preschool children in Chengdu, China

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Objective China has a high burden of tuberculosis and latent tuberculosis infection (LTBI). The aim of this study was to analyse the results of tuberculin skin test (TST) of 3865 healthy preschool children in Chengdu, China and estimate the prevalence of LTBI among them.
Methods A multi-stage stratified cluster sampling method was used to conduct the survey in kindergartens in Chenghua District, Chengdu. The results of TST were read after 72 h and analyzed.
Results 3,865 healthy preschool children completed TST test between Nov 2020 and Jan 2021 and were included in the present analysis. The age of the participants ranged from 2.4-7.3 years (median 3.36±0.956 years), of which 2,093 (54.15%) were younger than 5 years. 245 children with TST indurations ≥ 10mm and the overall LTBI prevalence among them was 6.33%. The LTBI rate was 6.59% (138/2093) for younger than 5 year and 6.04% (107/1772) for older than 5 years, the difference was not statistically significant (χ^2 =0.498, P>0.05). The LTBI rate was 11.11% (3/27) for children with close contact history with family tuberculosis patients and 6.31% (242/3838) for children without close contact history with family tuberculosis patients, the difference was not statistically significant χ^2 =0.391, P>0.05). The LTBI rate was 6.33% (240/3791) for Han children and 6.76% (5/74) for the minority, the difference was not statistically significant (χ^2 =0.000, P>0.05).
Conclusions Healthy preschool children should also be considered as an important target population for LTBI screening and stronger measures are still needed to decrease the prevalence of LTBI among them.

关键字 latent tuberculosis infection, preschool children

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The First Chinese Family of Inherited Chromosomally Integrated Human Herpesvirus-6A in the Age of Metagenomic Next Generation Sequencing

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Background Human herpesvirus 6 is a ubiquitous beta herpesvirus that is divided into two species (HHV-6A and HHV－6B). HHV6 have been associated with a number of serious diseases in immunocompromised individuals including ataxia, hypersomnia, mild dementia, encephalitis and seizure. HHV-6 have been shown to integrate their genome into the telomeres of both somatic cells and germ cells resulting in any offspring arising from that germ cell carrying a copy of HHV-6 in each of their own cells. The latter condition is referred to as inherited chromosomally integrated HHV-6 (iciHHV-6) and presents in approximately 1% of the human population which does not indicate active infection. HHV-6 is revealed to be the second most commonly detected target in evaluation studies of the FilmArray Meningitis/Encephalitis panel after enteroviruses. In that case, establishing HHV-6 infection based solely on detection from CSF can be difficult. In this study, we would like to present a family of iciHHV6A firstly given the metagenomic next generation sequencing (mNGS) positive result for HHV-6A from cerebrospinal fluid (CSF).

Methods A Chinese family of iciHHV6A from department of Infectious Diseases, Beijing Children’s Hospital was analyzed.

Results A one-month-old child was referred to our ward with 19-day history of fever. He had been treated with ceftriaxone before admission to our center. On examination, His temperature was 38℃, he appeared weakness and had bulging fontanelle. The complete blood count showed WBC, 18460/ml; neutrophils, 6810/ml; lymphocytes, 4980/ml; hemoglobin, 9.2g/dl; and platelets, 1012,000/ml. Inflammatory markers were elevated with CRP 141.09 mg/L and ESR 76mm/h. The CSF white blood cells was 26/ml, monocytes was 22/ml, multinuclear cell was 4/ml, protein level was 817mg/L, glucose level was 3 mmol/L, culture was negative. A brain contrast-enhanced magnetic resonance imaging (MRI) scan revealed abnormal meningeal enhancement. A presumptive diagnosis of bacterial meningitis was made and hence he was started on Meropenem. Then his fever subsided. Blood herpes virus PCR was performed, blood HHV6 copy was 3.02x10^5/ml. mNGS of CSF sample tent to be positive for HHV-6A (reads 221). Because of high HHV6 copies in blood and HHV-6A from CSF, we suspected iciHHV6 and HHV6A is not the cause of meningitis. Then we performed blood HHV6 PCR of mother and father. Mother also had a high copy with 1.26x10^5 copies/ml while his father had negative result. Further, investigation of HHV-6 U86 PCR of hair follicle from the patient, older sister, older brother, mother, grandmother, grandfather was done. Results showed positive in patient, older sister and mother’s hair while negative in others. Thus, we confirmed the family of iciHHV6A for we detected HHV-6A DNA from the somatic cells both from mother, older sister and patient. The child had good outcome without treat with antivirals. To the best of our known, this is the first Chinese iciHHV-6A family.

Conclusions Clinicians should differentiate HHV-6 viral activation or integration if HHV-6 DNA is detected from CSF, especially HHV-6A from neonate. Further tests need to be done for confirming HHV-6 status which could ultimately help reduce unnecessary antiviral therapy.

关键字 inherited chromosomally integrated human herpesvirus-6; somatic cells; metagenomic next-generation sequencing

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“Klebsiella.pnuemoniae” or “Klebsiella.varricola” ? : The First Pediatric Community Acquired Klebsiella.varricola Bacterial Meningitis identified by Metagenomic Next Generation Sequencing

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Background This study aimed to report the clinical characteristics of Klebsiella.varricola (K. varricola) identified by metagenomic next generation sequencing (mNGS) which caused pediatric community acquired bacterial meningitis in a previous healthy toddler and further illustrate the microbiological and genomic features of the causative strain.

Methods A one-year-old girl was admitted to our hospital and diagnosed as community acquired bacterial meningitis. “K.pnuemoniae” was isolated from the cerebral spinal fluid by MALDI-TOF MS. Antimicrobial susceptibility was determined by broth microdilution method. mNGS result tended to be K. varricola. Genetic information was obtained by whole-genome sequencing and bioinformatics analysis.

Results The child admitted to our hospital presenting with “fever and vomiting for one day”. She had meningeal irritation and a spinal dermal sinus tract on the occipital region. She had pleocytosis in CSF, low level of glucose and high level of protein. In addition, two “K.pnuemoniae” were isolated from the cerebral spinal fluid both from other hospital and our hospital. The two isolates were susceptible to all antibiotics. However, the mNGS identified K.varricola (reads 22, coverage 0.12%). When the whole-genome sequencing of the strain 20-27 was compared with the nine genomes of the K.varricola strains, the ranges of average nucleotide identity and digital DNA-DNA hybridization values were 98.98% ± 1.42% - 99.63% ± 0.94% and 91.6% - 97.0%, respectively which highly supposed to be identified as K.varricola. Phylogenetic analysis of K.varricola unique genes, yggE and rpoB, were also conducted. And the phylogenetic trees clearly showed that the strain 20-27 clustered with K.varricola. There was no high virulence gene found. Thus, the patient was finally diagnosed as community acquired K.varricola bacterial meningitis. The girl took good response to the Meropenem. To the best of our known, this is the first case of pediatric community acquired bacterial meningitis caused by K.varricola.

Conclusions Antibiotic-susceptible K.varricola could cause pediatric community acquired bacterial meningitis. And the misidentification of K.varricola as K.pnuemoniae by certain methods of clinical microbiology might lead to underestimate the percentage of K.varricola infection potentially. mNGS may raise an effective role in the identification between K.varricola and K.pnuemoniae.

关键字 bacterial meningitis, pediatric, Klebsiella.varricola, metagenomic next generation sequencing

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Analysis of clinical characteristics and anti-tuberculosis treatment of neonatal tuberculosis

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Background
Neonatal tuberculosis includes congenital tuberculosis and tuberculosis in the newborn. This study was to analyze the clinical features of neonatal tuberculosis and to explore the efficacy and safety of first-line anti-tuberculosis drugs in the treatment of neonatal tuberculosis, which could help to provide help for early identification and correct diagnosis and treatment of neonatal tuberculosis.

Method
The clinical data of 48 infants with neonatal tuberculosis in Children's Hospital of Chongqing Medical University from January 2010 to December 2020 were analyzed retrospectively.

Results
There were 24 males (50.00%) in the 48 infants, and the median age of onset was 14.5 days (0.5-22.0 days) . The mothers of 41 infants (95.0%) were found to have tuberculosis. 33 (68.75%) infants were congenital tuberculosis and 15 (31.25%) infants were non-congenital tuberculosis. Compared with the non-congenital tuberculosis group, there was no significant difference in other aspects except that the age of onset was earlier and the contact history was more definite in the congenital tuberculosis group. The most common clinical manifestations were fever （72.92%）, shortness of breath（66.67%） and cough（56.25%）. The positive rates of acid-fast bacilli smear and Mycobacterium tuberculosis culture were 54.17% and 41.18% respectively. The positive rate of tuberculin skin test, tuberculosis infection T cell spot test was 33.33%, 65.52%. Combined with imaging findings, 47 cases (97.92%) had pulmonary involvement, 22 cases (45.83%) had abdominal involvement, and 18 cases (37.50%) had intracranial involvement. 36 (75.00%) cases were given isoniazid, rifampicin, pyrazinamide and or not combined with ethambutol or streptomycin for anti-tuberculosis treatment, and 13 (36.1%) cases were given glucocorticoids Hormones. The overall incidence of adverse reactions to first-line anti-tuberculosis drugs was 41.67% (15/36). The most common adverse reaction was drug-induced liver injury (12/36, 33.3%), and other adverse reactions included hearing impairment (2/36, 5.56%) , severe intestinal reaction, hyperuricemia, and skin rash were each in 1 case. In the drug-induced liver injury group, the proportion of full-term infants, abdominal distension and bile acid levels at admission were significantly higher than those in the non-drug-induced liver injury group (P<0.05). In the 48 infants, 24(50.00%) infants improved and stopped drug treatment after anti-tuberculosis treatment without relapse, 9(18.75%) infants were still under treatment, 8(16.67%) infants died and 7(14.58%) infants lost follow-up.

Conclusions
The clinical manifestation of neonatal tuberculosis is not specific, and diagnosis should be combined with maternal tuberculosis history, tuberculosis contact history, etiological evidence and imaging examination, etc. The incidence of adverse reactions in the treatment of neonatal tuberculosis with first-line anti-tuberculosis drugs was

high, and the main adverse reaction was drug-induced liver injury. Early detection and anti-tuberculosis treatment are expected to slow down the disease progression and reduce the mortality.

关键字 Tuberculosis, Congenital tuberculosis, Neonate, Infant

分类：15. Infectious Disease 感染
1143

The Role of Cas6 Interacting Proteins in the Host Defense Against Mycobacterium tuberculosis

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The immune response of host resistance to Mycobacterium tuberculosis (MTB) plays an important role in the pathogenesis of Tuberculosis (TB), and apoptosis is a key part in host defense against MTB. This study is based on the previous study of the results that MTB Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)/Cas (CRISPR-associated proteins) system protein Cas6 can induce apoptosis of THP-1 cells, then targets on G-protein coupled receptor 133 (GPR133) and pan-leukocytic surface molecules CD84 (Leukocyte differentiation antigen CD84). In vitro and in vivo experiments were conducted to investigate the role of Cas6 interacting proteins GPR133 and CD84. In vitro experiments, bone marrow derived microphages (BMDMs) were collected from GPR133$^{-/-}$ mice and CD84$^{-/-}$ mice, then apoptosis levels were detected after Cas6 protein stimulation in order to clarify the role of GPR133 and CD84 in the process of apoptosis. In vivo experiments, the ability to resist MTB infection of GPR133$^{-/-}$ mice and CD84$^{-/-}$ mice were detected to further validate the role of GPR133 and CD84 in host immune response against MTB.

Objective: To clarify the role of Cas6 interacting proteins GPR133 and CD84 in host immune response against MTB.

Methods: 1) The apoptosis rate of BMDMs from GPR133$^{-/-}$ mice and CD84$^{-/-}$ mice induced by Cas6 protein: CRISPR/Cas9 technology was used to generate GPR133$^{-/-}$ mice and CD84$^{-/-}$ mice, BMDMs from two kinds of knockout mice and wild type mice were stimulated with Cas6 protein, and the apoptosis rate of BMDMs and the level of TNF-α and IL-6 were detected. 2) The different ability to resist MTB infection between GPR133$^{-/-}$ mice and CD84$^{-/-}$ mice: MTB reference strain H37Rv was used to infect GPR133$^{-/-}$ mice, CD84$^{-/-}$ mice and wild-type mice. The differences of lung MTB Colony-Forming Units (CFU) from GPR133$^{-/-}$ mice, CD84$^{-/-}$ mice and wild-type mice were compared to explore the role of these two proteins in MTB infection.

Results: 1) In the study of the difference of BMDMs apoptosis rate between GPR133$^{-/-}$ mice and CD84$^{-/-}$ mice induced by Cas6 protein: there was no significant difference in the apoptosis rate and level of TNF-α and IL-6 secreted by BMDMs from GPR133$^{-/-}$ mice and wild-type mice. In CD84$^{-/-}$ mice, the apoptosis rate and the levels of TNF-α and IL-6 were decreased following Cas6 treated. 2) In the study of the difference in ability to resist MTB infection between GPR133$^{-/-}$ mice and CD84$^{-/-}$ mice: compared with wild-type mice, the lung CFU was similar in GPR133$^{-/-}$ mice, but significantly increased in CD84$^{-/-}$ mice.

Conlusion: GPR133 has no obvious effect on the apoptosis process induced by Cas6 protein, and GPR133$^{-/-}$ mice's ability to resist MTB infection is similar to the wild-type mice. CD84 promotes the apoptosis of macrophages induced by Cas6 protein, and the ability to resist MTB infection is reduced in CD84$^{-/-}$ mice.

关键字 Tuberculosis, Apoptosis, Cas6, CD84, GPR133

分类：15. Infectious Disease 感染
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Neonatal Dubin-Johnson Syndrome and its differentiation from Biliary Atresia

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Objective: To determine if liver biochemistry indices can be used as biomarkers to differentiate neonatal Dubin-Johnson syndrome (nDJS) patients from biliary atresia (BA).
Methods: Patients with nDJS (confirmed by DNA sequencing) previously treated at our center were studied retrospectively. The patients' liver chemistries, measured before the age of three months, were compared to those with BA. Patients were randomly assigned to a discovery and a verification cohort to screen for biomarkers that distinguish nDJS from BA. The predictive values of laboratory features were calculated by receiver operating characteristic (ROC) curve analyses.
Results: A cohort of 53 nDJS patients were recruited for this study. Among these, 13 patients presented with acholic stools, and 14 patients underwent diagnostic cholangiography or needle liver biopsy to differentiate from BA. Thirty-five patients in this cohort, with complete biochemical information measured during the neonatal period, were compared with infants with cholangiography confirmed BA (n=133). The levels of TB, DB, ALT, AST, TBA, ALP and GGT in nDJS were significantly lower than that in BA. The area under the curve value (AUC) for ALT and AST were 0.910 and 0.936, respectively, in the discovery cohort. In the validation cohort, 13/15 patients were positive among the nDJS group, while 10/53 were positive among the BA controls ($P < 0.00001$) with ALT as a biomarker (cut-off value 75 IU/L), while 13/15 patients were classified as nDJS and none were classified positive among the BA group (13/15 vs 0/53, $P<0.00001$) with AST as a biomarker (cut-off value 87 IU/L). None of the eight nDJS patients who underwent liver biopsy exhibited melanin-like pigment deposits.
Conclusions: We have assembled and investigated the largest cohort of neonatal Dubin-Johnson syndrome patients reported to date. We found that nDJS patients could be distinguished from BA patients by using the level of serum AST as a biomarker. This finding may be clinically useful to triage cholestatic nDJS patients from unnecessary invasive procedures.

关键字 jaundice; ABCC2; cholestasis

分类：15. Infectious Disease 感染
1154

Population pharmacokinetics-pharmacodynamics of ceftazidime in neonates and young infants: Dosing optimization for neonatal sepsis

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Ceftazidime is a third-generation cephalosporin with high activity against many pathogens. But the ambiguity and diversity of the dosing regimens in neonates and young infants impair access to effective treatment. Thus, we conducted a population pharmacokinetic study of ceftazidime in this vulnerable population and recommended a model-based dosage regimen to optimize sepsis therapy. Totally 146 neonates and young infants (gestational age (GA): 36－43.4 weeks, postnatal age (PNA): 1－81 days, current weight (CW): 900－4500 g) were enrolled based on inclusion and exclusion criteria. Ceftazidime bloods samples (203) were obtained using the opportunistic sampling strategy and determined by the high-performance liquid chromatography. The population pharmacokinetic-pharmacodynamic analysis was conducted by nonlinear mixed effects model (NONMEM). A one-compartment model with first-order elimination best described the pharmacokinetic data. Covariate analysis showed the significance of GA, PNA, and CW on developmental pharmacokinetics. Monte Carlo simulation was performed based on above covariates and minimum inhibitory concentration (MIC). In the newborns with PNA ≤ 3 days (MIC=8 mg/L), the dose regimen was 25 mg/kg twice daily (BID). For the newborns with PNA >3 days (MIC=16 mg/L), the optimal dose was 30 mg/kg three times daily (TID) for those with GA ≤37 weeks and 40 mg/kg TID for those with GA >37 weeks. Overall, on the basis of the developmental population pharmacokinetic-pharmacodynamic analysis covering the whole range of neonates and young infants, the evidence-based ceftazidime dosage regimens were proposed to optimize neonatal early-onset and late-onset sepsis therapy.

关键字 Ceftazidime, Neonatal sepsis, Neonate, Young infant, Population pharmacokinetics, and Pharmacodynamics

分类：15. Infectious Disease 感染
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Latamoxef for Neonates With Early-Onset Neonatal Sepsis: A Study Protocol for a Randomized Controlled Trial

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Early-onset neonatal sepsis (EONS), a bacterial infection that occurs within 72 hours after birth, is associated with high likelihood of neonatal mortality. Latamoxef, a semi-synthetic oxacephem antibiotic developed in 1980s, has been brought back into empirical EONS treatment in recent years. In the preliminary work, we established a population pharmacokinetics (PPK) model for latamoxef in Chinese neonates. Moreover, in order to better guide clinical treatment, we conducted dose simulation and found that ascending administration frequency could improve the target rate of 70% of patients having a free antimicrobial drug concentration exceeding the MIC during 70% of the dosing interval (70% fT>MIC). Accordingly, this study is aimed to compare the 70% fT>MIC, efficacy and safety between conventional regimen and PPK model regimen for rational use of latamoxef in EONS treatment.

A single-blind, multicenter randomized controlled trial (RCT) for latamoxef will be conducted in Chinese EONS patients. Neonates (≤3 days of age, expected number = 114) admitted to the hospital with the diagnosis of EONS and fulfilling inclusion and exclusion criteria will be randomized (ratio of 1:1) to either a conventional regimen (30 mg/kg q12h) or model regimen (20 mg/kg q8h) latamoxef treatment group for at least 3 days. Primary outcome measure will be 70% fT>MIC and secondary outcome indicators will be the latamoxef treatment failure, duration of antibiotic therapy, changes of white blood cell count (WBC), C-reactive protein (CRP) and procalcitonin (PCT), blood culture results during administration and incidence of adverse event (AE)s. Assessments will be made at baseline, initial stage of latamoxef treatment (18-72h) and before the end of latamoxef treatment. Ethical approval of our clinical trial has been granted by the ethics committee of the Beijing Children’s Hospital (ID: 2020-13-1). Written informed consent will be obtained from the parents of the participants. This trial is registered in the Chinese Clinical Trial Registry (ChiCTR 2000040064).

It is hoped that our study will provide a clinical basis for the rational clinical use of latamoxef in EONS treatment.

关键字 latamoxef, early-onset neonatal sepsis, neonate, randomized controlled trial, study protocol

分类：15. Infectious Disease 感染
1200

Relationship between bacterial DNA load and clinical characteristics in children with pertussis

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Summary: Background To identify association between Bordetella pertussis DNA load and clinical characteristics. Methods 504 children with pertussis hospitalized in Shenzhen Children's Hospital from May 2017 to Oct 2018 were analyzed retrospectively. Patients were divided to two groups,according to the result of culture and drug susceptibility test,complications,treatment,severity and vaccination status.The different of DNA load between two groups were compared,and the correlation between the DNA load and WBC count, age ,length of stay in hospital were explored, and the changing trend of DNA load during the treatment were analyzed. Result The DNA load of each group were compared.Patients with positive in culture was higher than those negative in culture (4.42 VS 2.99), patients with resistance with erythromycin was higher than those sensitive with erythromyc(6.28 VS 5.13), patients who received compound sulfamethoxazole(SMZco) was higher than those who did not (5.50 VS 4.40) ,patients with severe pertussis was higher than those with non-severe pertussis(5.07 VS 4.38),patients who were not vaccinated was higher than those who were vaccinated(4.67 VS 4.37), and the difference was statistically significant (P<0.05).Boedetella pertussis DNA load was pasitively correlated with WBC count(r=0.18, P<0.01) and length of stay in hospital(r=0.20, P<0.01),and negatively correlated with age(r=-0.11, P=0.02).In the SMZco group,no decrease in DNA load was observed before SMZco treatment, and the DNA load was significantly decreased after SMZco treatment (P<0.05).Conclusion The DNA load of Bordetella pertussis is related to the results of culture and drug susceptibility test. Its change trend in the process of treatment is helpful to select the antibiotics and judge the occurrence of severe pertussis.

关键字 pertussis;children;DNA load;clinical characteristics

Category: 15. Infectious Disease 感染
1392

Natto intake was associated with B. subtilis bacteremia among children undergoing chemotherapy for childhood cancer

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Abstract Content Background
Although Bacillus species can cause bacteremia in immunocompromised children, it is unknown whether Japanese food, natto fermented by Bacillus subtilis can be provided safely during chemotherapy for children with childhood cancer. The purpose of this study was to identify whether natto intake could be a risk factor for B. subtilis bacteremia in children undergoing chemotherapy.

Methods A retrospective matched case-control study was conducted at Tokyo Metropolitan Children's Medical Center in Japan between April 2012 and June 2020. The study included pediatric patients aged under 15-year-old who received chemotherapy for childhood cancer. Patients received hematopoietic stem cell transplantation were excluded. Cases with B. subtilis bacteremia were compared with matched control for natto intake. Diet information within 7 days from the date of blood culture drawn was collected from medical records. Multivariate logistic regression tests were performed to define the risk factors of B. subtilis bacteremia.
Results A total of 23 Bacillus subtilis bacteremia cases were identified, and 92 controls were matched. Patients with B. subtilis bacteremia were treated with antibiotic therapy and all of them had good clinical and microbiological responses. Natto intake within 7 days from the date of blood culture in cases and controls were 78% and 50%, respectively. The odds ratio of natto intake for B. subtilis bacteremia was 3.6 (95% confidence interval [CI], 1.2 to 10.5). In multivariable logistic regression tests to control for neutropenia, we found that B. subtilis bacteremia was related with natto intake (odds ratio, 3.3; 95% CI, 1.1 to 9.6).

Conclusion Natto intake was associated with B. subtilis bacteremia during chemotherapy for childhood cancer in children.

Key words natto intake, B. subtilis bacteremia, chemotherapy for childhood cancer
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分类：15. Infectious Disease 感染
1394

One Case of Cerebral Paragonimiasis in Children

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Objective To investigate the clinical characteristics and causes of misdiagnosis of cerebral paragonimiasis in children. **Methods** The diagnosis and treatment process, including laboratory test and imaging examination, of a child with cerebral paragonimiasis with unilateral limb weakness as the main clinical manifestation is reported and retrospectively analyzed to summarize the experience. **Results** The clinical manifestations of cerebral paragonimiasis are diverse. Cranial imaging suggests space-occupying lesion and elevated eosinophils. Combined with epidemiological history, completing parasite immunological examination is helpful for timely definitive diagnosis. **Conclusion** Attaching importance to the increase of eosinophils in hematology, strengthening the understanding of imaging of parasitic infections, timely completing parasite antibody detection, and improving the vigilance for parasitic infections are the main measures to reduce misdiagnosis.

关键字 Cerebral paragonimiasis; Magnetic resonance imaging (MRI); Eosinophils

Category: 15. Infectious Disease 感染
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The Role of High Dose Vitamin D as Adjunctive Treatment for Childhood Pneumonia: A Systematic Review

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Abstract Content Pneumonia accounts for 16% of children's deaths in many hospitals in low-income countries. Recently, Vitamin D supplementation has been considered as a potential strategy for pneumonia treatment: to boost adaptive immune system activity and reduce excessive inflammation effects that may help children recover from pneumonia. As death due to pneumonia could be preventable, the development of effective new interventions is essential to reduce childhood mortality. This study aims to investigate the role of vitamin D as adjunctive treatment in children with pneumonia.

Methods A systematic literature review was conducted in the English language published study using PubMed, Cochrane, and Google Scholar search within the last ten years comprising randomized control trials (RCTs) only. The studies investigated the effect of Vitamin D supplementation as an adjunctive treatment for pneumonia in children. PRISMA statement is displayed in this study.
Results We included 9 RCTs conducted in low-income countries that involved 1917 children. We observed some significant roles of Vitamin D for childhood pneumonia; three studies stated significant result on reducing hospitalized duration, two studies displayed the effectiveness of vitamin D in preventing recurrence of pneumonia, one study showed improvement of ARDS severity. Only one study showed adverse impact of vitamin D, which gave minimal symptoms.
Conclusion The role of high dose vitamin D as adjunctive treatment for childhood pneumonia remains inconclusive, but we observed significant outcomes in some trials. Further trials are needed to strengthen the study result.

Key words vitamin D, pneumonia, children, adjunctive therapy,
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分类：15. Infectious Disease 感染
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Pediatric Deep Venous Thrombosis Associated with Staphylococcus aureus Osteomyelitis

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Objective, To evaluate clinical features of children with Deep venous thrombosis (DVT) associated with acute hematogenous osteomyelitis (AHO) caused by Staphylococcus aureus.
Design, We reviewed a 4-year medical records of patients with DVT of AHO conclusive caused by Staphylococcus aureus (S. aureus) retrospectively and we compared clinical and laboratory characteristics of AHO with or without DVT, and patients whose DVT dissolved within or more than 3 weeks. also We compared characteristicss of AHO whose DVT dissolved within 3 weeks with those six patients whose DVT dissolved more than 3 weeks.
Results, 87 AHO patients were admitted during four years period. Nineteen of 87 (22%) patients had DVT. For DVT patients, median age was 9 years (range, 6 mouths-15 years). 74% (14/19) patients were boys. Patients were all previously healthy with no underlying chronic illness or immunodeficiency or other risk factors for DVT. None of the patients in this study reported previously thrombophilia or family history of thrombosis. All cases were community acquired (CA). Methicillin-susceptible Staphylococcus aureus (MSSA) accounted for 58% (11/19). Most of DVT sites were lower extremity and all venous thrombus occurred adjacent to the infection site. Femoral vein and common femoral vein were both the two most affected vein (9 cases, respectively). Pulmonary embolism was reported in four of nine cases who performed chest CT. Eighteen (95%) patients received anticoagulation therapy with low molecular weight heparin. Inferior vena cava (IVC) filters was placed in one patient whose DVT was fluttering for prophylaxis against pulmonary embolism. Seven of the 13 (54%) with available data had complete resolution of DVT within three weeks of anticoagulation therapy. None of patients required rehospitalization for bleeding or recurrent of DVT. Comparative analysis found patients with DVT were older (9 v. 4 years old, P=0.005). CRP, PCT, platelet count were lower in patients with DVT($P \leqslant 0.001$). D-dimer, fibrinogen were higher. The rate of admission to ICU, positive blood culture, multifocal were higher in DVT($P<0.05$). And hospitalization was longer in those with DVT than without (33.5 v. 14.2 days, P=0.033). We compared seven patients whose DVT dissolved within 3 weeks with those six patients whose DVT dissolved more than 3 weeks and found there’s no difference between age, inflammatory marker, bacteremia rate, MRSA rate and ICU admission rate.
Conclusion, We reported nineteen cases of DVT in association with AHO conclusive caused by S. aureus in pediatrics of Chinese population. More than twenty percent of patients with S. aureus AHO developed DVT in present study. MSSA accounted more than half. More than half of DVT patients were related to MSSA infection. Patients with DVT had more higher inflammation maker, ICU admission rate and prolonged hospital stay. More than half of patients were with earlier resolution of DVT in three weeks, those four patients whose DVT resolved in one week underwent just 1-2 weeks low molecular weight heparin (LMWH) treatment had no recurrent of DVT.

关键字 venous thrombosis, Staphylococcus aureus, osteomyelitis, children

分类：15. Infectious Disease 感染
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Prevalence and antibiotic resistance of bacteria isolated from cerebrospinal fluid among children with bacterial meningitis in China from 2016 to 2018: a multicenter retrospective study

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Methods: Data of 1193 cerebrospinal fluid bacterial isolates from children with BM admitted to thirteen children's hospitals in China from 2016 to 2018 were analyzed retrospectively.
Results: Of the 1142 patients with PBM, 65.9% (753) were less than 1 year old, among which more than two-thirds (513, 68.1%) were younger than 3 months. The most prevalent pathogens causing PBM were Staphylococcus epidermidis (16.5%), Escherichia coli (12.4%) and Streptococcus pneumoniae (10.6%). The age group of under 3 months was at a relatively high risk of infection by Escherichia coli (116/523; 22.2%), Enterococcus faecium (75/523; 14.3%), Staphylococcus epidermidis (57/523; 10.9%), and Group B Streptococcus (55/523, 10.5%). However, the age group of more than 3 months was at a relatively high risk of infection by Staphylococcus epidermidis (140/670; 20.9%), Streptococcus pneumoniae (117/670; 17.5%), and Staphylococcus hominis (57/670; 8.5%). More than 93.0% of E. coli isolates were sensitive to cefoxitin, piperacillin/tazobactam, cefoperazone/sulbactam, amikacin, carbapenems, while the resistance rates to ceftriaxone, cefotaxime and ceftazidime were 49.4%, 49.2% and 26.4%, respectively. From 2016 to 2018, the proportion of methicillin-resistant Coagulase-negative Staphylococcus (MRCoNS) isolates declined from 80.5% to 72.3%, while the frequency of penicillin-resistant S. pneumoniae (PRSP) isolates increased from 75% to 87.5%. The proportion of extended-spectrum β-lactamase (ESBL)-producing E. coli fluctuated between 44.4% and 49.2%, and the detection rate of ESBL production among K. pneumoniae ranged from 55.6% to 88.9%. The resistance of E. coli strains to carbapenems was 5.0%, but the overall prevalence of carbapenem-resistant (CR) K. pneumoniae was high (54.5%).
Conclusions: The resistance of CoNS to methicillin and the high incidence of ESBL production among gram-negative Enterobacteriaceae posed a critical challenge to infection control. Carbapenem-resistant K. pneumoniae isolates are a large issue for the treatment of children with PBM.

关键字 Bacterial meningitis, pediatric, bacterial pathogens, antimicrobial resistance

分类：15. Infectious Disease 感染
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Thymic density changes in post-chemotherapy sepsis of children with acute lymphoblastic leukemia and its diagnostic value

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Background As the central lymphoid organ for T cell development, thymus plays an important role in maintaining homeostatic cellular immunity. The function of thymus may be associated with relative complications in post-chemotherapy acute lymphoblastic leukemia patients. The present study aimed to investigate the diagnostic value of thymic density on CT in post-chemotherapy sepsis of patients with acute lymphoblastic leukemia. **METHODS** A total of 59 acute lymphoblastic leukemia cases and 36 control subjects in Shenzhen Children Hospital from January 2019 to August 2021 were selected for the study, and were divided into acute lymphoblastic leukemia (ALL) group and control group. Acute lymphoblastic leukemia patients were divided into sepsis group (22 cases) and non-sepsis group (37 cases) according to whether had post-chemotherapy sepsis. Retrospectively analyzed the chest CT image, blood routine examination (including neutrophil count and CRP) and lymphocyte subsets test (including the whole T cell absolute counts, lymphocytes CD4 absolute counts, lymphocytes CD8 absolute counts and lymphocyte absolute counts) in 3 days of all the subjects. The independent sample t-test was used for measurement data and Pearson xˆ2 was used for nominal variables. ROC curve method was used to analyze the diagnostic value of thymic CT value in post-chemotherapy sepsis of patients with acute lymphoblastic leukemia. **RESULTS** ①The thymic CT value (35.76±24.63HU) in acute lymphoblastic leukemia group was significantly lower than that in control group (49.96±15.71HU) ,and the difference were statistically significant(P＜0.05).②The thymic CT value (16.52±21.28HU) in sepsis group was lower than that in non-sepsis group (47.2±18.79HU) ,and the difference were statistically significant(P＜0.05).③The area under the ROC curve (AUC) of thymic non-contrast CT value (0.907) was higher than other values. The cut-off value of thymic CT value was 35.38HU, the sensitivity was 81.1%, and the specificity was 86.4%. **CONCLUSIONS** The low thymic CT value can be used as early reference index of abnormal cellular immunity in children. When the thymic CT value is lower than 35.38HU, the risk of post-chemotherapy sepsis in ALL may increase.

关键字 children; acute lymphoblastic leukemia; sepsis; thymus; tomography;density

分类：15. Infectious Disease 感染
1659

儿童腹膜透析相关腹膜炎的罕见病因：缺陷乏氧菌

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Abiotrophia defective (*A. defectiva*) is a frequently reported clinical infection; however, it is rarely implicated in peritoneal dialysis-related infections in peritonitis patients. This article reports a rare case of peritoneal dialysis-related peritonitis caused by *A. defectiva* in a child. A 12-year-old Chinese child with end stage renal disease who presented with abdominal pain and vomiting and a cell count 567.10×10^6/L cells of which 84% were polymorphonuclear. The PD effluent was cultured using the standard operating protocols, and the organism was identified as A. defectiva by matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS). The patient responds well to ceftazidime and vancomycin, ten days later, the PD effluent culture and white cell count returned negative. This is the first case report *A. defectiva* PD-Peritonitis in an end stage renal disease child reported in Asia. Clinicians and microbiologists should pay greater attention to this organism and its pathogenic potential in patients with PD-Peritonitis, whose pathogenicity often is underestimated.

关键字 Abiotrophia defectiva, PD-Peritonitis, MALDI-TOF MS, child

分类：15. Infectious Disease 感染
1683

Clinical and Laboratory Characteristics and Factors Associated with Disease Severity in Pediatric Patients with Hemorrhagic Fever With Renal Syndrome Caused by Hantaan Virus

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Objective: To understand the clinical features of hemorrhagic fever with renal syndrome (HFRS) in children, to analyze factors related to disease severity and prognosis, to provide basis for diagnosis and prognosis of HFRS in children.
Methods: A total of 206 children with HFRS who were admitted to the Department of Infectious Diseases, Xi 'an Children's Hospital from January 2012 to December 2020 were included. According to the clinical classification standard, the patients were divided into mild (79 cases), moderate (84 cases), severe (22 cases) and critical (21 cases). Feature selection was adopted to screen appropriate variables through information gain method, and variable attribute >0.1 factor was selected for logistic regression. The prediction model was established by multivariate logistic regression analysis. ROC curve was used to analyze the predictive efficacy of the model of critical illness and/or death and ICU admission and/or death in children, and the predictive factors of logistic regression were visualized by histogram. All data were analyzed by SPSS25.0, Orange3.24.1 and Medcalc statistical software18.1. P < 0.05 was statistically significant.
Results: The majority of all patients are male, the average age was 8.20±3.37 years, and the rural population was the majority, the onset season was mainly from October to December in autumn and winter. Multifactor logistics regression analysis was performed on clinical variables related to critical and/or death and 5 laboratory indicators (APTT, BUN, PT, PCT, INR) screened by information gain > 0.1: pleural effusion, hypotension, cerebral edema, and/or cerebral hernia are independent risk factors for critical and/or death; BUN, PCT and PT are independent risk factors for critical and/or death. The clinical variables of admission to ICU and/or death and 5 laboratory indicators (BUN, Cr, PCT, APTT, CK-MB) screened by information gain > 0.1 were determined by multifactor logistics regression: pericardial effusion, pleural effusion, oliguria, and hypotension were independent risk factors for ICU admission and/or death; BUN and PCT are independent risk factors for ICU admission and/or death. BUN and PCT associated with both outcomes were selected to construct the prediction model. ROC curve showed that BUN+PCT combined to predict the AUC of critical and/or dead children was 0.89 (95%CI: 0.84-0.93, P<0.01), sensitivity 90.5%, specificity 78.9% .BUN+PCT combined to predict the AUC of ICU admission and/or death was 0.93 (95%CI: 0.89-0.96, P<0.01), sensitivity 96.2%, specificity 80%. They were better than BUN or PCT BUN alone or PCT alone.The predictors of logistic regression were visual by line graph. The results showed that BUN+PCT could accurately predict critical and/or death and admission to ICU and/or death.
Conclusion: The clinical manifestations of HFRS in children are often atypical.In the areas with high incidence of HFRS, Children with fever, platelets to reduce, positive proteinuria, and renal damage should be highly vigilant, to avoid missed diagnosis, misdiagnosis and mistreatment. Combined detection of BUN and PCT has important diagnostic value for early identification of critical type, ICU admission and death cases in HFRS children.

关键字 儿童；HFRS；临床症状；临床结果

分类：15. Infectious Disease 感染
1700

Trend analysis of Antimicrobial Resistance of Staphylococcus aureus Causing infection among children at the first Hospital affiliated of Anhui medical University in the Last 10-Year Period Reports (2010-2020), the north-western part of eastern China

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Objective: This study investigated the epidemiology and drug resistance of Staphylococcus aureus (S. aureus) isolates among children at the first Hospital affiliated of Anhui medical University in the north-western part of eastern China in order to obtain epidemiologic and antimicrobial resistance data that can guide for the selection and development of anti-infection treatments.Methods: A total of 536 S. aureus strains were isolated from children between January 2010 and December 2020 at the first Hospital affiliated of Anhui medical University. The strains were identified by mass spectrometry or VITEK 2 Compact system . The Kirby-Bauer method and VITEK 2 Compact system were used to analyze the antimicrobial susceptibility.
Results: In this report, we analyze the trends in antimicrobial resistance of Staphylococcus aureus according to the last 10-year-period reports. Not like the noteworthy decreasing of MRSA isolate in the infection of adults is encouraging, but there has been concern about the considerable proportion in children, as it has greatly enhanced from 17.2% (2010) to 29.3% (2020), peaking at 33.4% in 2014. Moreover, it has stably contributed to about 30% of S. aureus infection in recent years, which indicated increased focus on infection prevention and stronger control interventions on children should be taken.It is encouraging that there is a decreasing MRSA proportion in the infection of children as well as better activity of non-beta-lactam agents in vitro in recent years.

关键字 Staphylococcus aureus, antimicrobial resistance

分类：15. Infectious Disease 感染
1717

The Periodic Law of Body Temperature in Children with Acute Mycoplasma Ppneumoniae Pneumonia and the Enlightenment of Artificial Intelligence

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Background
This paper intends to elaborate the hypothesis of "body temperature cycle law of pathogenic microbial infection" through the study of the law of body temperature change in children with Mycoplasma pneumoniae pneumonia. To study the relationship between fever and pathogenic microorganisms(PMs) in children with acute Mycoplasma pneumoniae(MP) pneumonia(MPP), and to explore the application prospect of artificial intelligence electronic temperature monitoring.
Methods
Among 1155 hospitalized children with acute MPP, 124 children were selected because their body temperature (BT) was accurately and continuously monitored every 2 hours during hospitalization. We established a decision support system for clinical diagnosis of community-acquired pneumonia in children based on big data. Two body temperature display systems were established in this system. The first body temperature display system was a 24-hour body temperature change curve table. The ordinate was body temperature and the abscissa was hour, a total of 24 hours a day. The second temperature display system was the curve table of daily maximum temperature (DMBT) and average temperature (DABT), with the ordinate of body temperature and the abscissa of day (calculated from the first day of admission). The characteristics and rules of waveform changes of 24-hour body temperature, daily maximum body temperature (DMBT) and daily average body temperature (DABT) were observed.
Fever cycle (FC) was defined as generally in 24 hours (start from 0:00 in the morning),the time interval from the highest temperature of the first fever to the highest temperature of the next fever, which was calculated in hours.The quantitative indexes such as fever cycle were calculated. Steady state phase (SSP): after children with normal immune function were infected by a certain pathogenic microorganism, the host and pathogenic microorganism were in a relatively stable equilibrium state. At this stage, the reproductive cycle rate of pathogenic microorganism was the same, and the toxin and exogenous heat source were released at the same reproductive cycle rate, causing periodic fever of the host clinically. Different pathogenic microorganisms had different reproductive cycles, so the fever cycle was also different.
Results
In this study, the average length of hospital stay of 124 children was 6.5 days, containing 19 fever cycle (FC), and the average fever cycle was 8.2 hours in the steady state phase (SSP). After 3 days of anti-Mycoplasma pneumoniae treatment, 99.19% of children's body temperature fell below 38 ℃, and 98.39% of children's body temperature returned to normal after 4 days of treatment.
Conclusion

The reproductive cycle of pathogenic microorganisms was similar to the ‘physiological cycle’ of women of childbearing age. And the reproductive cycle of pathogenic microorganisms was consistent with the fever cycle of host steady state phase (SSP). The biological law of the periodic fever in the steady state phase (SSP) of the host caused by pathogenic microorganisms was defined as ‘the Periodic Law of Body Temperature (PLBT)’. It is suggested that pediatricians can monitor fever cycle of children with respiratory system infection by artificial intelligence electronic thermometer. And then determine and / or exclude certain pathogenic microorganism by combining clinical symptoms and signs, general routine tests and other information. According to the temperature feedback, we can judge the accuracy of diagnosis and the effectiveness of treatment, and modify the diagnosis and treatment plan in time. The value of the Periodic Law of Body Temperature (PLBT) of pathogenic microbial infection was to make up for the defects of current clinical laboratory detection technology.

关键字 acute Mycoplasma pneumoniae pneumonia, fever cycle, steady state phase, electronic thermometer, periodic law of body temperature

分类：15. Infectious Disease 感染
1732

Distribution characteristics of disease types and epidemic prevention effect of 51533 hospitalized children in pediatrics of tertiary hospitals in Nanjing in recent 12 years

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Background
To study the distribution characteristics of disease types and their relationship with age, year, season and other factors of 51533 hospitalized children (except newborns) in pediatrics of two tertiary hospitals in Nanjing in recent 12 years. And through the comparison before and after the epidemic, the protective effect of Xinguan epidemic prevention on children's health was analyzed.
Method
A total of 51533 hospitalized children from January 2009 to July 2021 were included, with the minimum age of 1 month and the maximum age of 16 years, with an average age of 2.91 years. There were 35698 pediatrics in hospital A and 15835 pediatrics in hospital B. The children were divided into 4 groups: Group I: 28 days < a < 1 year old group. GroupⅡ: 1-year-old ≤ a < 3-year-old group. Group Ⅲ: 3 ≤ a < 6 years old group. Group Ⅳ: ≥ 6 years old group. The disease diagnosis was based on the national clinical classification of diseases version 2.0, and the first diagnosis was taken for all diseases.
Result
From January 2009 to July 2021, 51533 hospitalized children were treated in the two medical pediatrics. Among the 35698 hospitalized children in pediatrics of hospital A, acute upper respiratory tract infection, acute bronchitis and acute bronchopneumonia accounted for 87.2% of the total number of hospitalized children. Among the 15583 hospitalized children in pediatrics of hospital B, acute upper respiratory tract infection, acute bronchitis and acute bronchopneumonia accounted for 86.3% of the total number of hospitalized children. Before the two hospitals from 2012 to 2019, the total number of hospitalized children in hospital A tended to be saturated. Hospitalized children in hospital B showed a rapid upward trend, and reached the peak in 2019. After COVID-19, the total number of hospitalized children was significantly reduced due to precise prevention and control, which showed the great achievements of COVID-19 prevention and control in China.
According to the diagnosis data of 51533 hospitalized children, the top five diseases in recent ten years are: 1.Acute bronchopneumonia; 2.Acute upper respiratory tract infection; 3. Acute bronchitis; 4.Other systemic diseases (diseases other than respiratory and digestive systems); 5.Digestive system diseases, etc. The proportions of them in hospital A were 49.32%, 19.21%, 18.63%, 8.07% and 4.76% respectively. The proportions in hospital B were 51.01%, 22.1%, 13.17%, 10.13% and 3.59% respectively. The proportion of respiratory infectious diseases in the 4 groups in hospital A was 82.60%, 89.51%, 91.91% and 83.32% respectively. In hospital B was 82.60%, 86.39%, 92.94% and 79.80% respectively. It could be very similar, and the proportion of the

third group is the highest, ranging from 91.91% to 92.94% respectively. The total number of hospitalization in all 4 groups decreased significantly in 2020 COVID-19. From the seasonal analysis, the hospitalization peak of children with acute bronchopneumonia and acute bronchitis was from November to January of the next year. Analysis of epidemic prevention effect: In 2020, epidemic prevention and epidemic prevention achieved remarkable results, and respiratory infectious diseases dropped dramatically. Taking hospital B as an example, the number of hospitalized children decreased by 55.35% in 2020 compared with the whole year of 2019. Compared with the same period in the first half of 2019, the first half of 2020 and 2021 decreased by 67.50% and 49.71% respectively.
Conclusion
Respiratory infectious diseases are the most common diseases in childhood. Preschool children are a high incidence of respiratory infectious diseases, and autumn and winter are the most frequent seasons. There are relatively few hospitalized children with digestive system diseases. COVID-19 epidemic prevention work significantly reduced the incidence of respiratory infectious diseases in children, indicating that prevention is more meaningful than treatment.

关键字 disease types, epidemic prevention, children, pneumonia, distribution characteristics

分类：15. Infectious Disease 感染
1753

Searching for risk factors and establishing predictive models for severe and critical hand foot and mouth disease

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Objective: Severe and critical hand foot and mouth disease (HFMD) patients have an acute onset and poor prognosis. This study intends to establish an appropriate risk prediction model by analyzing the blood biochemical indicators of patients. Methods: A total of 3204 patients with HFMD were enrolled in this study, including 2131 mild patients, 962 severe patients and 111 critical patients. We analyzed the data of each group through univariate statistical analysis, and screened out the variables that had important contribution to the discrimination of each group.Then, binary logistic regression analysis was used to establish a suitable prediction model. Results: With the aggravation of HFMD patients' condition, the blood content and risk warning ability of 7 indicators of SP, DP, NEUT%, TP, GLB, RBP and Glu were significantly increased. The average prediction accuracy of the established models for Mild/Severe, Severe/Critical and Severe/Critical were 82.89%, 96.16% and 89.37%, respectively, and the AUROC were 0.8722 (95%CI, 0.8583-0.8861), 0.9499 (95%CI, 0.9339-0.9659) and 0.7913 (95%CI, 0.7471-0.8356), respectively.Conclusion: SP, DP, NEUT%, TP, GLB, RBP and Glu could be used as risk factors for severe and critical HFMD patients. The predictive model established by us could be used for the differential diagnosis of Mild/Severe and Mild/Critical and Severe/Critical.

关键字 风险因子　手足口　预测模型

分类：15. Infectious Disease 感染
1785

Prevalence and antimicrobial susceptibility of klebsiella pneumoniae carried in healthy children

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Background: The bacterium Klebsiella pneumoniae of family Enterobacteriacea is a well-known opportunistic pathogen that colonizes intestinal and respiratory tract. While K. pneumoniae is a common cause of nosocomial and community-acquired infections in susceptible hosts, little is known about the population structure of this bacterium. Thus it is likely that the prevalence of K. pneumoniae isolate from carriers and clinic patients, when combined to their antimicrobial susceptibility, might provide some insight into pathogenic Klebsiella prevention and control.
Methods: A total of 100 fecal samples were collected from healthy children. K. pneumoniae were isolated using macconkey agar medium. For the genomic analysis, all isolates were chosen for whole-genome sequencing by platform Illumina Hiseq PE150. Multilocus sequence typing (MLST) analysis was performed by sequencing seven housekeeping genes (gapA, infB, mdh, pgi, phoE, rpoB, tonB). For antimicrobial susceptibility identification, in silico antibiograms were predicted by Resfinder (version 4.0), the Resfinder database contains antibiotics aminoglycoside, beta-lactam, colistin, fluoroquinolone, fosfomycin, fusidic acid, glycopeptide, macrolide, lincosamide and streptogramin B (MLS), nitroimidazole, oxazolidinone, phenicol, pseudomonic acid, rifampicin, sulphonamide, tetracycline and trimethoprim associated resistance genes.
Results: Occurrence of K. pneumoniae in healthy children was 33.0% (33/100). The 33 K. pneumoniae isolates were subtyped into 24 sequence types (STs). Except for ST1536 (9.1%), ST3271 (9.1%), ST20 (6.1%), ST295 (6.1%), ST592 (6.1%), ST981 (6.1%), and ST1805 (6.1%), other STs were accounted for 3.0% (1/33) of isolates respectively. All isolates carried fosfomycin associated genes, and aminoglycoside (10.5%), beta-lactam (97.4%), fluoroquinolone (94.7%), MLS (2.6%), phenicol (2.6%), sulphonamide (7.9%), tetracycline (13.2%) and trimethoprim (2.6%) associated resistance genes were found in isolates from healthy children.
Conclusions: These data provide epidemiological support for the proposal that the distribution of sequence types of k. pneumoniae carried in healthy children was relatively dispersed. And the isolates from in healthy children were largely carried antibiotic resistances genes.

关键字 Klebsiella pneumoniae, Healthy children, Prevalence, Antimicrobial susceptibility

分类：15. Infectious Disease 感染
1792

Isolation and Analysis of biological Characteristics of New Delhi Metal β-lactamase Positive Bacteria from Children in China

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Background: New Delhi metallo-β-lactamase, a metallo-β-lactamase carbapenemase type, mediates resistance to most β-lactam antibiotics including penicillins, cephalosporins, and carbapenems. Especially in children, the rate of NDM is higher than that of other carbapenemase-resistant factors and its proportion is also higher than that in adults. Therefore, it is important to detect blaNDM genes in children's clinical samples as quickly as possible and analyze their characteristics. **Method**: The bla NDM genes in children's clinical samples were detected by recombinase-aided amplification (RAA) assay which operates in a one-step reaction tube at 39° C for 5-15 min. The sensitivity of the RAA assay was 20 copies, and the various sample types without bla NDM genes were not been amplified. The antimicrobial susceptibility of the blaNDM-positive isolates was tested by VITEK 2 compact system and MIC. The 16S sequencing was used to identify strains. **Results**: This method was used to detect bla NDM genes in 118 children's samples, 12 of which were tested positive by both RAA and standard PCR. To further investigate the characteristics of carbapenem-resistant bacteria carrying bla NDM in children, 18 carbapenem-resistant bacteria were isolated from the 12 samples , among them, 6 strains of Klebsiella pneumoniae, 3 strains of Escherichia coli, 3 strains of Citrobacter freundii, 2 strains of Acinetobacter baumannii, , 1 strain of Klebsiella oxytoca, and 1 strain of Acinetobacter junii. It is worth noting that there are three samples, more than one kind of bacteria and blaNDM gene were isolated in the same case. **Conclusions**: Most of these isolates were resistant to cephalosporins, cefoperazone-sulbactam, piperacillin-tazobactam, ticarcillin-clavulanic acid, aztreonam, co-trimoxazole, and carbapenems, but sensitive to tigecycline and amikacin. The susceptibility results of these children are consistent with their history of antibiotic use, blaNDM-1 and blaNDM-5 were the two main subtypes in these samples. The common existence of blaNDM and multi-drug resistance genes presents major challenges for pediatric treatment.

关键字 New Delhi metallo-β-lactamase,recombinase-aided amplification assay,Children

Allergy

过敏

Category: 1. Allergy 过敏
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Changes and significance of regulatory B cells in children with allergic asthma receiving mite-specific immunotherapy

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Abstract Content To investigate the changes of Regulatory B cells (Breg) in allergen immunotherapy in children suffering from mite allergic asthma and discuss the possible significance in the treatment.

Methods We enrolled 20 patients suffering from mite allergic asthma and undergoing build-up phase mite subcutaneous immunotherapy (SCIT) for 4-6 months. The blood was taken for testing before SCIT and at the end of the build-up phase. (1) the proportion CD19+CD24highCD27+Breg, Th1, Th2, Th17, Treg cells and the expression of Breg-related cytokines CD80, CD86, CD1d were tested by flow cytometry; (2) IL-10, TGF-β, IFNG, T-bet, IL-4, GATA3, IL-17A, RORγt, FOXP3 mRNA levels were detected in peripheral blood by real-time fluorescent quantitative PCR; (3)IL-10 and TGF-β concentrations were tested by ELISA in peripheral plasma.

Results (1) The ratio of CD19+CD24highCD27+Breg, IL-10 mRNA , transcription factors T-bet, GATA3, and RORrt mRNA and IL-10 and TGF-β protein levels in peripheral plasma , were significantly increased at the end of the the build-up phase than before the treatment($P<0.05$);(2) At the end of the build-up phase, the proportion of Th1, Th2, Th17 ,Treg cells in CD4+ T cells and the cytokines CD80, CD86, CD1d did not change significantly ($P>0.05$).

Conclusion When children with asthma who are allergic to mites receive SCIT treatment, the number of Bregs and IL-10-mediated immune regulation are the main factors in the build-up phase. Treg may not play a key role in this phase.

Key words Regulatory B cells (Breg); allergic asthma; mite allergic; Allergen-specific Immunotherapy (AIT)

Reference

分类：1. Allergy 过敏
68

Cumulative evidence for association of acetaminophen exposure and allergic rhinitis in children

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Background: Several studies have linked acetaminophen exposure to the risk of allergic rhinitis in children, with controversial results. We conducted a systematic review and meta-analysis to summarize the current evidence on the association between acetaminophen exposure and allergic rhinitis in children.
Methods: A systematic search of PubMed, Embase, Cochrane Library, and Web of Science was conducted up to February 1, 2021. We included observational studies that examined the association between acetaminophen exposure and the risk of allergic rhinitis in children. Two reviewers independently extracted data and assessed study quality. Summary odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using random effects meta-analysis.
Results: A total of 17 studies with 869,582 participants were included. Analysis showed that acetaminophen exposure was associated with an increased risk of allergic rhinitis in children (odds ratio [OR]: 1.54; 95% confidence interval [CI]: 1.41-1.70). Further analysis revealed that acetaminophen exposure in the first year after birth was associated with an increased risk of allergic rhinitis in children (OR: 1.34; 95% CI: 1.21-1.49). Also, exposure to acetaminophen in the past year was positively associated with the risk of allergic rhinitis in children (OR: 1.74; 95% CI: 1.48-2.04). The risk of allergic rhinitis was greater for children who had acetaminophen exposure once per month over the past year (OR: 1.90, 95% CI: 1.60－2.26) compared to once per year (OR: 1.28, 95% CI: 1.11－1.48).
Conclusions: With our meta-analysis, we provide the evidence that exposure to acetaminophen is associated with an increased risk of allergic rhinitis in children. In addition, acetaminophen exposure in early life and acetaminophen exposure in the past year are positively associated with the risk of allergic rhinitis in children. Future research is needed to evaluate whether the association is causal.

关键字 Acetaminophen, Allergic rhinitis, Meta-analysis, Risk factors

分类：1. Allergy 过敏
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A comprehensive analysis of cross-reactivity to the major pollens, food allergens, and components in patients with allergic diseases in southern China

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Background: Pollen allergens is an important contributor to allergic diseases, with varying patterns and frequency of allergens according to the geographical location studied.
Objective: In the present study, we aimed to characterize the prevalence of molecular components of the common pollen allergens and investigate the co-sensitization and cross-reactivity of allergen components and cross-reactive carbohydrate determinants (CCD) in Chinese pollen-sensitized patients with allergic diseases.
Methods: Serum samples from 165 pollen-sensitized patients with allergic diseases were tested for 19 allergen crude extracts and their components in Guangdong Province, China, using the component-resolved diagnosis(CRD), and the potential associations between allergens and their components were described.
Results: Among those positive simples for mugwort, 11 (18.0%), 15 (24.6%), and 15 (24.6%) were positive for Art v 1, Art v 2, and Art v 3, respectively. Among the 40 patients positive for birch, Bet v 2 had the highest positive rate (40.0%). For the 67 patients sensitized to ragweed, only five(7.5%) of them were positive for Amb a 1. There were 62 patients sensitized to walnut. Their components had a lower positive rate(all less than 15%). We used a hierarchical cluster and optimal scale analysis to divide the 19 allergens and CCD into seven different sensitization clusters. Meanwhile, Spearman's rank correlation analysis showed a significant association in sensitization between CCD and allergen crude extracts, as well as a low correlation between CCD and allergen components. Meanwhile, the levels of Jug r 3 were strongly correlated with Art v 3 ($r=0.78$; $P<0.001$).
Conclusions: In our present study, the positive rate of pollen allergen components was not high, which might be caused by cross-reaction.

关键字 Component-resolved diagnosis; Pollen; Walnut; China

分类：1. Allergy 过敏
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Exploring the role of basophil activation test in evaluation of therapeutic efficacy of omalizumab and subcutaneous immunotherapy in children with allergic asthma and rhinitis

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Objective:

It aims to detect basophil activation ratio (%$CD63^+$) in peripheral blood of children with allergic asthma and rhinitis by using Flow cytometry (FCM), so as to analyze the application values and clinical relevance of the Basophil Activation Test (BAT) in monitoring therapeutic efficacy of omalizumab and subcutaneous immunotherapy (SCIT).

Methods:

It was a prospective study. We enrolled the children who attended the pediatric asthma clinic in the Second Hospital of Tianjin Medical University from Octorber, 2018 to May, 2019. A total of 49 children who were newly diagnosed as moderate asthma and rhinitis sensitized by Derf were selected and accepted conventional treatment for 6 months. Among them, 35 patients received standardized SCIT (SCIT group), 7 patients received omalizumab treatment (omalizumab group) and 7 patients received only conventional treatment (control group). Using Derf extracts in the concentration of 1μg/ml, 10μg/ml and 100μg/ml as the stimulus, basophils were obtained by the gates CD123 and HLA-DR. %$CD63^+$ measured by BAT, the serum immunological indexes (sIgE, TIgE, sIgE/TIgE), skin prick tests (SPT), FEV1%pred in pulmonary ventilation function, exhaled nitric oxide (FeNO), children asthma control test (C-ACT) and pediatric asthma quality of life questionnaire (PAQLQ), visual analogue scale (VAS) and pediatric rhinoconjunctivitis quality of life questionnaire (PRQLQ) were detected before and after treatment in 3 groups and their internal connections were analyzed.

Results:

1. The optimal stimulating concentration of dust mites was 100 μg/ml. The average levels of %$CD63^+$ in the concentrations of 1μg/ml, 10μg/ml and 100μg/ml showed an increasing concentration-dependent trend overall ($p<0.05$). There was no significant difference in %$CD63^+$ among three groups before treatment ($P>0.05$). Six months later, %$CD63^+$ in SCIT group and omalizumab group were lower than before, and %$CD63^+$ in the two groups were lower than control group ($p<0.05$).
2. There was a positive correlation between %$CD63^+$ and SPT grade in Spearman rank correlation analysis ($p<0.05$). %$CD63^+$ was positively correlated with sIgE, sIgE / TIgE and VAS, and negatively correlated with C-ACT in Pearson linear correlation analysis ($p<0.05$). %$CD63^+$ was not correlated with TIgE, FEV1%pred and FeNO ($P> 0.05$).
3. After 6 months, the level of C-ACT in SCIT group and omalizumab group became higher than before, and C-ACT in the two groups were higher than that in control group ($p<0.05$). PAQLQ became higher than before, and PRQLQ became lower than before in omalizumab group ($p<0.05$).

Conclusions:

After receiving SCIT or omalizumab treatment, the symptoms of children with asthma and rhinitis have been improved. %$CD63^+$ measured by BAT, can be used as a biomarker to evaluate the efficacy of SCIT and omalizumab and has good clinical relevance in assessing the severity of symptoms.

关键字 Basophil activation test, Omalizumab, Subcutaneous immunotherapy, Allergic asthma, Rhinitis

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The age, sex, and geographical distribution of self-reported asthma triggers in children with asthma in China

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Background
Asthma can be exacerbated by many triggers, and the heterogeneity of asthma triggers is clear among children with asthma. This study describes asthma triggers using a large-scale electronic dataset from the smartphone-based Chinese Children's Asthma Action Plan (CCAAP) app and aims to examine the difference in asthma triggers among different subgroups of children with asthma.
Methods
Data from the smartphone-based CCAAP app between February 22, 2017, and November 23, 2020, were reviewed, and children with asthma who reported their asthma triggers were enrolled. Eight common asthma triggers were listed in the software: upper respiratory infection, allergen sensitization, exercise, emotional disturbances, pungent odors, air pollution/smog, weather change, and tobacco smoke. We compared the incidence of asthma triggers among different subgroups (<6 years vs. 6-17 years; boy vs. girl; eastern region vs. central region vs. western region).
Results
We enrolled 6835 patients with self-reported asthma triggers. When compared by sex, boys had a higher proportion of exercise-triggered asthma than girls (boys vs. girls, 22.5% vs. 19.7%, P<0.05). The proportion of patients <6 years of age with upper respiratory infection (URI)-triggered asthma was higher than that of patients 6-17 years of age (<6 years vs. 6-17 years, 80.9% vs. 74.9%, P<0.001). Patients 6-17 years of age were more likely than patients <6 years of age to report five of the asthma triggers: allergen sensitization (<6 years vs. 6-17 years, 26.6% vs. 35.8%, P<0.001), exercise (<6 years vs. 6-17 years, 19.3% vs. 23.7%, P<0.001), pungent odors (<6 years vs. 6-17 years, 8.8% vs. 12.7%, P<0.001), air pollution/smog (<6 years vs. 6-17 years, 9.4% vs. 16.2%, P<0.001), and tobacco smoke (<6 years vs. 6-17 years, 3.5% vs. 5.3%, P<0.001). In subgroups based on geographical distribution, asthma triggering of allergen sensitization was reported to be the most common in patients from the eastern region (eastern region vs. central region vs. western region, 35.0% vs. 24.6% vs. 28.0%, P<0.001). Exercise-triggered asthma was found to be the most prevalent among patients from the central region (eastern region vs. central region vs. western region, 21.6% vs. 24.8% vs. 20.4%, P<0.05). However, the proportion of patients with air pollution/smog as an asthma trigger was the lowest among those from the western region (eastern region vs. central region vs. western region, 14.1% vs. 14.1% vs. 10.8%, P<0.05).
Conclusions
Children with asthma present different types of asthma triggers, both allergenic and nonallergenic. Age, sex, and geographical distribution affect specific asthma triggers. Preventive measures can be implemented based on a patient's specific asthma trigger.

关键字 Asthma trigger; Asthma; Children; Age; Sex; Geographical

分类：1. Allergy 过敏
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Clinical characteristics and compliance analysis of sublingual immunotherapy for children allergic diseases

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Objective The investigation summarized the clinical characteristics and compliance status of children allergic diseases with standardized sublingual immunotherapy(SLIT), and analyzed the relevant factors influencing compliance. Method Retrospective reviewed the relevant clinical data of the follow-up of allergic diseases, summarized the relevant clinical characteristics, including gender, age, allergic disease diagnosis, parents' education of children, etc., and further discussed the main factors affecting SLIT compliance. Results There were 950 children, including 667 boys (70.21%), 283 girls (29.79%), were enrolled in this studywith an average age (6.95 ± 2.33). In the 950 children, 150 childrenunderwentwith single allergic disease(15.79%), whilethe rest 800 children suffered with mixed allergic diseases (84.21%).456 children were from families that both parentswere all low-educated (48.00%), while 308children were from the families both parentswereacquiredgood education(32.42%).and the rest 186 children were from families that only one parent was acquired good eduction (19.58%). There were 256 total compliance, compliance rate was26.95%. Gender, age, parental education, and diagnosis of allergic diseases were the main factors affecting SLIT compliance.All were correlated with SLIT compliance, statistical comparisons were all differ significantly, $p < 0.05$. A total of 694 SLIT cases were prematurely terminated. Among them, 271 cases (39.05 %) were due to poor outcome. In 248 cases(35.73%), patients gave up due to inconvenient of the treatment. In 168 cases (24.21%) patients, feeling the symptom improved enough, premautely stopped the treatment without doctor's consent. Seven cases (1.01%) were stopped due to adverse reactions. In dropout cases(including withdrawal and loss to flow up), time duration of prematurely termination varied greatly, in which 516 cases occurred within 4 months after the beginning of treatment, accounting for 74.35% of the total dropout cases. Conclusions In our hospital, children allergic diseases with SLIT prefer to male, low-age and patients with mixed diseases. Boy, high age, diagnosis of mixed diseases and parents were highly educated children had good SLIT compliance.

关键字 children; allergic diseases; sublingual immunotherapy; compliance; influencing factors

Category: 1. Allergy 过敏
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Natural History and Predictors for Persistence of Immediate-type Egg Allergy in Chinese Children

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Abstract Content Egg allergy is one of the most common food allergies in childhood with increasing prevalence in Hong Kong. Among Chinese preschoolers, shellfish (15.8%), egg (9.1%) and peanut (8.1%) were the leading causes of adverse food reactions. In a comparative study funded by EuroPrevall, sensitization to egg was amongst the top three foods in Chinese children living in Hong Kong and Guangzhou while it was uncommonly seen in Chinese from Shaoguan as well as Russian and Indian schoolchildren. Egg being an important source of protein in weaning diet for infants is commonly found in processed foods and baked goods. Accidental ingestion of egg or egg-containing foods is common, and such imposes anxiety and stress on egg-allergic children and their families. While there were many studies on its optimal diagnosis, there was limited data on predictors for the natural history of egg allergy in Asian populations. Previous studies reported specific IgE levels, age of first intake of egg and skin prick test results to predict outcomes of egg allergy. This study aimed to characterize the clinical course and outcome of children with egg allergy and identify its prognostic factors.

Methods This study recruited children younger than 18 years old with egg allergy who were referred to the allergy clinic of our university-affiliated teaching hospital between January 2003 and December 2017. The inclusion criteria for subjects included: (a) history of allergic reactions (e.g. hives, facial, eyelid or lip swelling, cough, dyspnea, wheeze, vomiting, diarrhea, abdominal pain, low blood pressure, drowsiness, loss of consciousness) within two hours following ingestion or skin contact with hen's egg; (b) wheal size to egg yolk and/or egg white >=3 mm larger than negative control by skin prick test (SPT); and (c) aged three years or older at first clinic consultation and followed for >=3 years. Patients who experienced delayed adverse reactions (>2 hours after egg ingestion or contact) were excluded. Demographics and personal and family history of allergic diseases of eligible subjects were retrieved from the hospital electronic patient record and/or medical record folders. SPT was performed with egg yolk, egg white, cow's milk, soybean, wheat and peanut as well as Dermatophagoides pteronyssinus (ALK-Abelló A/S, Hørsholm, Denmark), with histamine and normal saline being included as positive and negative controls respectively. Egg allergy diagnosis was made by suggestive clinical history after egg ingestion and >=3 mm wheal by SPT. Egg allergy was considered to be resolved when subjects acquired oral tolerance to egg with the absence of adverse reactions after reintroduction of regular egg ingestion at home for three months or longer, or tolerated a graded dose oral food challenge to hen's egg. In both categories, subjects must tolerate hen's egg at an amount appropriate to their age and weight. The natural course of egg allergy from the first allergic reaction was estimated using Kaplan-Meier curves. The relationship between different demographic, clinical and disease-related factors and the cumulative probability of egg allergy persistence was analyzed using log rank test.

Results Seventy-six patients with median (interquartile range [IQR]) age of 8.9 (6.3-13.0) years met the recruitment criteria, with 52 (68.4%) being male. The median (IQR)

age at first egg-allergic reaction was 1.0 (0.7-1.7) years, with 44 (57.9%) patients presented initially before two years of age. The main presenting features included urticaria (90.8%) and angioedema (53.9%), while 13 (17.1%) patients had anaphylaxis. Ninety percent of patients had family history of allergic diseases. Regarding baseline SPT results, 33 patients had >=6 mm wheal to egg yolk while 37 patients had >=6 mm wheal to egg white. Twenty-five (32.9%) patients had >=6 mm wheal to both egg yolk and egg white. Fifty-four (71.1%) patients developed tolerance to egg at a median (IQR) duration of 36.0 (27.3-52.0) months while 22 (28.9%) patients had persistent egg allergy. Patients with concomitant peanut allergy and those experienced the first allergic reaction at >=1 year old were more likely to have persistent egg allergy (P=0.015 and 0.027 respectively). SPT wheal >=6 mm to egg yolk as well as egg yolk and egg white were also predictors for egg allergy persistence (respective P<0.001 and 0.001 by log rank tests).
Conclusion This study shows that the majority of Chinese children with immediate-type egg allergy are able to tolerate egg upon long term follow-up. Wheal size of SPT to egg yolk as well as both egg yolk and white, concomitant peanut allergy and occurrence of first allergic reaction after infancy are possible predictors for egg allergy persistence in children. (funded by Hong Kong Institute of Allergy Research Grant)

Key words Egg allergy, natural history, persistence
Reference Available upon request.

Category: 1. Allergy 过敏
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Formulation and Pilot Testing of Recipes for Double-blind Histamine Challenges in Chinese Subjects with Possible Shrimp Allergy

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Abstract Content Histamine intolerance (HIT) is caused by a disequilibrium of histamine intake as well as its production and degradation in the body. These patients present with features of histamine overactivity such as skin itching, rashes, flushing and gastrointestinal upset. They can also develop more severe reactions such as wheeze and shortness of breath (bronchospasm) as well as dizziness and loss of consciousness (hypotension, shock). A high index of suspicion and meticulous dietary history are needed to identify patients with possible HIT. Like food allergy, a double-blind, placebo-controlled challenge with histamine-containing food is the gold standard for HIT diagnosis. Nonetheless, there is limited research on the relevant recipes and protocols for HIT in Asian populations. This study aimed to develop a recipe for double-blind histamine provocation and evaluate its concordance with existing HIT biomarkers and usefulness for diagnosing HIT.

Methods Chinese subjects with history of adverse food reactions after shrimp ingestion were subjected to skin prick test (SPT) and/or serum specific IgE assays for shrimp as well as double-blind, placebo-controlled shrimp challenge to ascertain their allergy status. Seventy-nine patients classified as shrimp-tolerant were recruited in this study for HIT workup. Forty-nine (62%) of these patients were suspected to have HIT based on histamine 50-skin-prick-test (HIS-50-SPT; wheal size >= 3 mm) and/or serum levels of diamine oxidase (DAO) (<= 10 U/mL). Seventeen of them gave informed written consent for double-blind, placebo-controlled histamine challenges. All these subjects underwent a 2-week low-histamine diet prior to the challenges. We offered a low-histamine breakfast and lunch respectively before each challenge. The actual histamine provocation took place on two separate days within a week with placebo (coconut-ginger pudding) and active (coconut-ginger pudding containing 0.5 mg/kg then 1.0 mg/kg of histamine hydrochloride) interventions being arranged in random sequence. A nurse unaware of the nature of such interventions assessed subjective and objective parameters at baseline, 20, 40 and 100 minutes after each dose. Our research staff recorded and scored possible HIT and allergy symptoms against a pre-developed system.

Results 17 subjects (5 males and 12 females) with mean (standard deviation [SD]) age of 29.3 (9.6) years completed the whole procedure. The mean (SD) HIS-50-SPT wheal size was 2.2 (2.3) mm and mean (SD) serum DAO levels were 2.3 (1.3) U/mL. These two HIT biomarkers did not correlate with each other. During the histamine-reduced diet, some subjects reported improvement of their allergic symptoms: gastrointestinal (24%), mucocutaneous (18%) and nasal (6%). The remaining subjects did not notice any difference in their symptoms. Following the double-blind histamine provocation, one subject was diagnose to have HIT (i.e. positive to histamine and negative to placebo) while one subject was negative to histamine but positive to placebo and 15 subjects did not react to both interventions. The most common histamine-related symptoms were rash (53%), pruritis (35%) and itching (18%). For placebo, subjects reported the

following symptoms: pruritis (47%), itching (18%) and rash (18%). Twelve percent of subjects reported bloating after ingestion of histamine-containing food but not in placebo. This pilot study could not evaluate the concordance between results of histamine provocation and existing HIT biomarkers because of the small number of HIT subjects being identified.
Conclusion This study devises a recipe and establish the protocol for double-blind, placebo-controlled histamine challenge in Chinese subjects. This recipe is palatable and well tolerated in our subjects, and a histamine-reduced diet followed by titrated provocation with histamine may be a possible approach to diagnose HIT in our population. (funded by Hong Kong Institute of Allergy Research Grant and Direct Grant for Research of The Chinese University of Hong Kong)

Key words Allergy, double-blind placebo-controlled food challenge, histamine intolerance, shrimp
Reference Available upon request.

Category: 1. Allergy 过敏
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Relationship between Demographics, Perinatal Factors and Early-life Exposures and Eczema Development in Chinese Infants

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Abstract Content Understanding the effects of prenatal and early life exposures on infantile eczema in specific region is important as early prevention strategies. In this study, we aim to determine early-life factors that predicted increased risk of childhood eczema during infancy in a Chinese birth cohort.

Methods This study was based on the prospective, observational SMART Baby birth cohort that recruited 120 Chinese mother-child pairs in Hong Kong from September 2017 to April 2021. Data on prenatal and early-life exposures were obtained from parent/guardian-administered questionnaire at antenatal, 1, 6 and 12 months of age, which further classified into non-modifiable and modifiable factors. Three eczema outcomes namely history eczema, current eczema and non-eczema were defined by parental-reported and physician-diagnosed during the study time points. Multivariable logistic regression were performed to estimate the association between exposures and infantile eczema using odd ratio (ORs) and 95% confidence interval (CIs) at significant p-value of 0.05.

Results The final analysis consisted of 96 mother-child pairs (49.0% [47] male, gestational age median=39 weeks, IQR=37-42). The incidence of history eczema was 21% (20), current eczema was 32.3% (31) and non-eczema was 46.9% (45). Infants with diagnosed-eczema and/or itchy rash were likely to have treatment of emollients (94.1%) and steroids (56.8%). After adjusting for confounding effects, multivariable analysis revealed that emergency cesarean delivery [aOR 8.62, 95% CI (1.48-50.19)] and maternal probiotic intake during pregnancy [aOR 6.73, 95% CI (1.45-31.21)] were associated with increased risk of history eczema that had been resolved before 12 months of age.

Conclusion Our study suggests that factors associated with infantile eczema are modifiable through lifestyle practices. Clinicians are encourage to discuss choice of delivery mode and its implication on child eczema with parents who intend to have children. (funded by Hong Kong Institute of Allergy Research Grant)

Key words Birth cohort, early-life exposures, eczema, risk factors
Reference Available upon request.

分类：1. Allergy 过敏
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Clinical characteristics and short-term prognosis of cow's milk protein allergy in children

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Background: To summary the clinical manifestation and analyze the laboratory change in children with cow's milk protein allergy (CMPA), to investigate the factors associated with the short-term prognosis of CMPA.
Methods: Children who had been diagnosed as CMPA and finished 6 months follow-up were enrolled during October 2019 through October 2020 from outpatients in the hospital of Capital Institute of Pediatrics. The data of personal history, family history and clinical symptoms were collected and necessary laboratory testing were completed for all patients.
Results: 115 children (71 boys, 44 girls) were finally enrolled with the first onset age at 6.5±3.6 months. The clinical manifestation occurred after eating food with milk, contacting milk and breastfeeding. Children's symptoms included cutaneous (101/115，87.8%), digestive (28/115，24.3%), respiratory (16/115，13.9%)and cardiovascular (1/115，0.9%) symptoms, and 23 children who ever had at least one anaphylaxis. Component resolved diagnosis (CRD) showed that 50% of children were sensitized to casein, 37% were sensitized to α-lactalbumin, 39% to β-lactoglobulin, and 38% to BSA. All children had a history of other allergic diseases or family allergies. The baseline of milk sIgE level, skin prick test reactions and positive α-lactalbumin sIgE were associated with the severity of clinical symptoms（P＜0.05）.
A total of 94 (81.7%) of 115 cow's milk allergic children finished 6 months follow-up. Cow's milk resolved in 24 children (25.5%), 70 children (74.5%) had persistent milk protein allergy. Baseline factors, including anaphylaxis with cow's milk and the severity of skin prick test reactions, were significantly associated with later resolution of cow's milk allergy（OR=3.34,95%CI：1.4～51.4；OR=2.3,95% CI：1.3～81.4.P＜0.05）.
Conclusion：The clinical manifestations of CMPA in children are varied, mainly skin systems, most were sensitized to at least one milk allergen component. Anaphylaxis with cow's milk and the severity of skin prick test reactions may predict a more severe course of milk allergy with late resolution. Serum sIgE detection, skin prick testing and allergen components shows an important role in the diagnosis and evaluation of CMPA.

关键字 cow's milk allergy; children; prognosis

分类：1. Allergy 过敏
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Allergen Sensitization among Children with Allergic Diseases in Shanghai, China: Age and sex differences

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Background:
The distribution of allergens has geographic characteristics. Local epidemiological data provide evidence-based strategies for the prevention and management of allergic diseases. Age and sex differences may exist in the prevalence of sensitivity to various allergens. We investigated the distribution of common allergens in allergic children in Shanghai, southeastern China.
Methods:
39,926 children 1 month to 18 years of age diagnosed with allergic diseases were tested for the presence of serum-specific Immunoglobulins E (sIgE) to 17 allergens common to this region, using a reversed enzyme allergosorbent test.
Results:
25,757 (64.5%) of the subjects showed elevated sIgE to at least one of the tested allergens. House mite and dust mite were the most common aeroallergens, while egg and milk were the most common food allergens. By age-group analysis, the positive rates of aeroallergens were higher at older ages. Several peaks of sensitization to food allergens were observed in children between 1year and 3 years of age for eggs, milk, nut, crab and shrimp. In addition, the sensitization to beef and mango was highest in children 3 to 6 years of age. The rate of positive sIgE detection was statistically different between males and females for all the tested allergens except cockroach, trees, beef and egg.
Conclusions:
House mite, dust mite, milk, and egg are major allergens in Shanghai. Children at younger age are more sensitive to food allergens, while increasing overall prevalence of sensitization can be found with increasing age. Boys have higher positive rates of sIgE responses than girls. Knowledge of the prevalence of allergen sensitization in different age groups and sex may help facilitate diagnosis and intervention efforts to mitigate the impact of allergic diseases in this large geographical region. This approach may be extrapolated to other regions.

关键字 Allergic disease; allergen; aeroallergen; children; Serum IgE; Sex difference; age difference

分类：1. Allergy 过敏
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Efficacy and adverse reactions of montelukast for treating children with rhinitis or asthma

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Introduction Montelukast has been used for a long time but the efficacy still needs more studies to prove. In 2020, the US FDA issued a black box warning about the risk of psychiatric events associated with montelukast. Moreover, the application is somewhat limited by concerns about its safety. More studies on the clinical efficacy and adverse reactions of montelukast still need to be taken in China
Aim This study aims to evaluate the efficacy and investigate the incidence of psychiatric events in children with asthma or rhinitis treated with montelukast in China.
Methods We retrospectively analyzed the application of montelukast in 2020 in Shanghai Children’s Medical Center. Basic information and neuropsychiatric events recorded through questionnaires.
Results Totaling 1654 patients were enrolled in our study. 91.8% of the participants reported that symptoms were improved while only 2 cases corresponded to deteriorated symptoms.
The overall rate of psychiatric disorders was 25.8%. Among the various neuropsychiatric adverse reactions, emotional problems and behavioral problems are more prominent (16.0%, 16.4%, respectively). No difference was found in each age group or difference sexes. Symptoms are mostly occasional and mild. The most frequently reported NEs were excitement (242,14.6%), followed by Irritability (231,16.0%).
Conclusion Montelukast was effective to relieve symptoms in children with asthma or rhinitis. Neuropsychiatric disorders as side effects of montelukast should not be overlooked. Risk management plans and epidemiological studies are needed to quantify the risk. Practitioners should be aware of the risk of neuropsychiatric events associated with montelukast use, and caregivers should also pay attention to it.

关键字 Adverse drug reactions; Montelukast; Psychiatric; Asthma; Rhinitis; Children; Safety

Category: 1. Allergy 过敏
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Airway nitric oxide in children with HDM-induced chronic rhinitis

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Abstract Content Background: To evaluate airway nitric oxide in children with HDM-induced chronic rhinitis

Methods Fifty-four children age 5-18 years with moderate to severe persistent chronic rhinitis were screened and received the HDM nasal provocation test. The demographic data and nasal symptoms evaluated by total nasal symptom score (TNSS) and visual analog scale (VAS) were recorded. Skin prick test (SPT) to common aeroallergens, fractional exhaled nitric oxide (FeNO), nasal nitric oxide (nNO), and blood test for specific IgE (sIgE) to house dust mite (HDM) was measured. Rhinitis severity was categorized as severe if the VAS score is more than 7.

Results Forty-eight children with house dust mite-induced allergic rhinitis were enrolled. The mean age of patients was 9.3 ± 2.4 years; 58% were male. SPT was positive in 46 children (96%): 32 children (70%) showed the positive result to the only HDM, 14 children (30%) were positive to HDM and other aeroallergens. sIgE to HDM showed positive results in 43 children (92%). nNO levels and VAS score were significantly correlated (r= 0.398, P=0.005). Children with severe chronic rhinitis had significantly higher nNO levels than those with moderate chronic rhinitis (1652 vs. 934 ppb, p=0.002). ROC analysis demonstrated the cut-off value of nNO for severe HDM-induced chronic rhinitis was 1350 ppb (AUC 0.764, 95%CI: 0.616-0.911, p= 0.002) with the sensitivity of 78% and the specificity of 71%. The level of FeNO in children who had HDM mean wheal diameter (MWD) > 8 mm was significantly higher than those with HDM MWD of 3-8 mm and those with a negative result (39.7 vs. 14.3 vs. 14.4 ppb; p=0.006, respectively). Children who had sIgE to HDM less than 0.35 KUA/L had significantly lower FeNO than those with sIgE to HDM >0.35-50 KUA/L and >50 KUA/L (9.5 vs 19.7 vs 40.4 ppb; p= 0.029, respectively).

Conclusion Cut-off value for the diagnosis of severe HDM-induced chronic rhinitis was proposed. Rhinitis children who had a higher degree of HDM sensitization had a higher level of FeNO.

Key words allergic rhinitis, nitric oxide, fractional exhaled nitric oxide, house dust mite

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Category: 1. Allergy 过敏
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Safety of Messenger RNA and Whole Inactivated COVID-19 Vaccines in Patients with Immediate Reactions to First-dose BNT162b2 and Other Polyethylene Glycol-containing Drugs

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Abstract Content Hypersensitivity reactions (HSRs) have been observed in those who received COVID-19 mRNA vaccines, and the culprit is thought to be the excipient polyethylene glycol (PEG) (molecular weight (MW)=2000 daltons).1 Anaphylaxis due to vaccines and drugs can be fatal. On the other hand, inappropriate concerns on vaccine allergy may lead to unnecessary delays and hesitancy in COVID-19 vaccination, and these can be important impediments against immune protection for individuals and control of the pandemic for the whole society.

Asparaginase and etoposide are effective chemotherapeutic agents for cancers. In addition to the COVID-19 mRNA vaccine, BNT162b2, PEG is contained in the pegylated asparaginase derived from native Escherichia coli (PEG-asparaginase) and etoposide (300-400 daltons for both).2 The allergenicity of PEG differs depending on its MWs. For cancer patients with past HSRs to PEG-asparaginase and etoposide, the potential for allergenic cross reactivity with COVID-19 vaccines remains unclear. Importantly, whether individuals who had HSRs to PEG-containing vaccines and drugs can safely receive the COVID-19 vaccines is not yet fully known. The aim of this study, COVA-P, was to investigate the clinical tolerance of COVID-19 vaccination in patients who developed immediate HSRs to PEG-containing vaccines and drugs.

Methods COVA-P was approved by the HKU/HKWC IRB (UW21-157) and registered at clinicaltrials.gov (NCT04800133). Patients who experienced HSRs within 4 hours after their first BNT162b2, PEG-asparaginase or etoposide infusions were enrolled into this prospective study after informed consent and assent. Basophil activation test (BAT) was performed using the Flow CAST® and reagent kits, which included the PEG 2,000 (BÜHLMANN Laboratories AG, Schönenbuch, Switzerland). Blood was incubated with a negative control, positive control (anti-IgE receptor antibody), PEG 2,000 and liposomal doxorubicin-PEG 2,000-3,500 complex separately in stimulation buffer. The activation marker, CD63, on basophils was measured by flow cytometry (Beckman Coulter Inc, Brea, USA). The test was considered positive if CD63 expression was >5%. Skin testing was avoided due to potential anaphylaxis-eliciting and accuracy concerns. Patients were given the option to receive the COVID-19 vaccines, BNT162b2 or Sinovac-CoronaVac (a whole inactivated vaccine with no PEG or polysorbate-80), by a graded approach (10%, or 0.03 mL of full dose, followed by 1-hour close monitoring prior to the remainder 90%, or 0.27 mL, injection) or a single full-dose administration. Participants were monitored for at least 1 hour after each injection. The study protocol required their reporting of no or any symptom in a diary for 7 days.

Results Three and 4 patients with immediate HSRs to BNT162b2 and to the PEG-containing chemotherapeutic agents (3 to PEG-asparaginase and 1 to etoposide),

respectively, were recruited. Except for mild allergic rhinitis and allergies to vaccines or drugs as aforementioned, they had no significant history of atopy or urticaria. Those with HSRs to the first-dose BNT162b2 had generalized urticaria within 1-3 hours that lasted several days for 2 patients, while 1 patient continued to have urticaria occasionally. Three participants had the blood cancer, acute lymphoblastic leukemia (ALL) diagnosed 6-16 years old while 1 had suprasellar and third ventricular mixed germ cell tumour diagnosed at age 10 years and received 6 cycles of carboplatin/etoposide alternating with ifosfamide/etoposide, radiotherapy and tumour resection. All of them developed systemic HSRs during their PEG-containing chemotherapy infusions and were labeled as having PEG-asparaginase or etoposide drug allergies.
BAT for 1 of the participants was indeterminant because of non-responder basophils. He received his second BNT162b2 by the graded approach. A small wheal developed at his lower back 1 hour afterwards, which resolved 30 minutes after cetirizine. He had urticaria at his legs the next day. BAT was positive to PEGs for a patient with PEG-asparaginase allergy, who decided to receive the Sinovac-CoronaVac even before the availability of the blood testing results. BAT for the other participants were negative. A total of 5 and 2 participants received BNT162b2 and Sinovac-CoronaVac (n=2), respectively. There was no moderate/severe reaction or serious adverse event during the 1-hour observational period or according to their 7-day diaries.
Conclusion Children and young adults who had immediate HSRs to a PEG-containing vaccine or chemotherapeutic agent were able to successfully receive the BNT162b2 or Sinovac-CoronaVac. These findings support the notion that allergy skin testing or BAT prior to COVID-19 vaccines is clinically unnecessary for these patients but may instead cause undue vaccination delay. Our study demonstrates that patients with HSRs to PEG-containing chemotherapeutic agents can safely receive the COVID-19 vaccines. The cellular mechanisms underlying adverse reactions to mRNA vaccines and polyethylene glycol deserve further research.

Key words COVID-19, vaccine, allergy, oncology, chemotherapy
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分类：1. Allergy 过敏
1267

Omalizumab in the treatment of refractory allergic asthma with allergic rhinitis in children: A case report

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OBJECTIVE: To explore the clinical efficacy and safety of omalizumab in the treatment of refractory allergic asthma with allergic rhinitis in children.
Methods: Retrospectively collect the clinical data of a child with refractory allergic asthma and allergic rhinitis who were treated in our hospital, and compared the changes in asthma symptoms and lung function before and after treatment.
Results: A 7-year-old male patient was admitted to the hospital mainly for ″repeated cough and wheezing for more than 3 years and exacerbated for 15 days″. In the past 3 years ago, due to ″repeated cough and wheezing for more than 1 year″, the child was diagnosed as ″1.Bronchial asthma 2.Pneumonia 3.Allergic rhinitis″, and was discharged after the hospitalization treatment improved. He did not take regular medications and still had coughing and wheezing.1 year ago, he regularly taking Budesonide/formoterol (160) twice a day, montelukast 5 mg 1/day. On average, it appears acute attacks such as cough, sputum, and runny nose after respiratory infections every month. So he was changed to 3 times a day, but it was still not well controlled. On admission to the hospital, the breath sounds in both lungs were thick, and phlegm sounds were heard. The rest of the system showed no abnormalities in the physical examination. Chest CT scan: Extensive expansion of the bronchi in both lungs, heavy infection in the middle lobe of the right lung, and mucus embolism in the expanded bronchi is not excluded. Other examinations: IgE: 1040KIU/L; specific allergen Aspergillus fumigatus sIgE 2.95 (grade 2) positive, Aspergillus fumigatus IgG antibody <31.25 AU/ml, IgM antibody 42.64 AU/ml; lung function: FEV1% predicted value 80.9%, FEF25 66.7%, FEF50 39.3%, FEF75 22.2%; The allergic bronchopulmonary aspergillosis are not excepted. After admission, he was given anti-infection and nebulization treatment. But he still had cough and wheezing. Repeat IgE: 426KIU/L. After excluding relevant influencing factors such as medication regimen and compliance, it was considered that although the child received a combination medication regimen containing a medium dose of ICS, the asthma was still not well controlled. According to the patient's total serum IgE level and body weight, omalizumab was injected subcutaneously once a month with 300 mg, and its effectiveness was judged after 16 weeks of planned use. After discharge from the hospital, the child regularly inhaled drugs and regularly injected omalizumab twice in the outpatient department. No related adverse reactions were seen. The child's cough and wheezing symptoms have improved significantly, and there is no obvious abnormality in the physical examination. It is believed that it can be reduced to twice a day, lung function: FEV1% predicted value 93.9%, FEF25 59.9%, FEF50 64.4%, FEF75 54.0%. In the follow-up, we will observe the changes in the symptoms and clinical indicators of the child during ICS reduction and regular treatment or dose reduction of omalizumab.
Conclusion: Omalizumab can significantly improve the clinical manifestations, lung function and quality of life in children with refractory allergic asthma. The corresponding course of treatment, potential benefits and adverse reactions still require a large sample of studies.

关键字 Omalizumab, Refractory allergic asthma, Allergic rhinitis

分类：1. Allergy 过敏
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Study on the Mechanism of YAP/FOXM1 Pathway in Children with Acute Asthmatic Induced by Viral Infection

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Abstract

Objective: To explore the effect of YAP/FOXM1 pathway in children with acute asthmatic induced by viral infection.
Methods: Sixteen healthy and SPF BALB/C female mice aged 6-8 weeks were divided into control group, asthma group, YAP induced group and YAP inhibited group according to randomly. The model of asthma was established with house dust mite, acute asthma attack was induced by Poly(I:C), and the expression of YAP was selectively inhibited by verteporfin. The lung tissue of mice was retained. The mRNA and protein expressions of YAP and FOXM1/SPDEF/Muc5AC were determined by real-time PCR , Western Blot and immunohistochemistry to investigate whether YAP affects the expression of FOXM1 and related pathways.
Results: 1. The mRNA and protein expressions of YAP in asthma group were significantly higher than those in control group, and the difference was statistically significant ($P<0.05$); The YAP induced group was significantly higher than the normal control group, asthma group and YAP inhibited group (all $P<0.05$). 2. The mRNA and protein expressions of mucus secretion-related transcription factor FOXM1 and downstream target genes SPDEF and MUC5AC in asthma group were significantly higher than those in control group ($P<0.05$); The YAP induced group was significantly higher than normal control group, asthma group and YAP inhibited group (all $P<0.05$). 3. The mRNA expression of IL-4 and IL-13 in asthma group was significantly higher than that in control group ($P<0.05$); The YAP induced group was significantly higher than control group, asthma group and YAP inhibited group (all $P<0.05$). The mRNA expression of IFN-γ in asthma group was significantly lower than that in control group ($P<0.05$). The YAP inducted group was significantly higher than that in control group, asthma group and YAP inhibited group (all $P<0.05$).
Conclusion: FOXM1 is a downstream target of YAP, and YAP promotes the proliferation and goblet metaplasia of bronchial epithelial cells through FOXM1/SPDEF/Muc5AC in virus-induced acute asthma.

关键字 YAP；FOXM1；Virus；Asthma

Category: 1. Allergy 过敏
1352

Safety and efficacy of wheat oral immunotherapy in wheat allergy children

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Abstract Content Background: Wheat allergy is a rising health issue among Thai children. Dietary restriction is the primary strategy for food allergies. Oral immunotherapy, on the other hand, may assist wheat allergy sufferers by promoting tolerance.
Objective:To evaluate the safety and efficacy of wheat oral immunotherapy protocol in children with IgE-mediated wheat allergy.

Methods The study was a retrospective review of children's medical records who underwent wheat OIT at the Pediatric Allergy and Immunology Unit, Ramathibodi Hospital, Mahidol University, between December 2015 and September 2021. All enrolled children were confirmed to have wheat allergies by the oral wheat challenge. The OIT protocol consists of a gradual increment of wheat flour every two weeks during the build-up phase until reaching the maintenance phase of 50 g of wheat flour. After one year of maintenance dose, an oral wheat challenge was conducted to evaluate wheat tolerance.
Results Eighteen children with IgE-mediated wheat allergy were enrolled (median age, 5.3 years; range, 2.4-10.4 years), and 14 (77.8%) were male. The most common presenting symptoms at wheat allergy diagnosis were anaphylaxis (61.1%). Median sIgE to wheat was 8.51 kUA/L (range 0.8-100 kUA/L). The median eliciting wheat dose was 1.8 g of wheat flour (equivalent to 234 mg of wheat protein). Moderate to severe allergic reactions occurred in 5 children (27.8%) in the build-up and 2 children (18.2%) in the maintenance phase. Only two children developed severe reactions requiring intramuscular epinephrine. Two children were dropped out during the build-up phase, 5 children were still in the build-up phase, and 11 children reached the maintenance phase. Three out of 11 children passed the oral wheat challenge with 100 g wheat flour within 2.4 years after initiation of OIT.

Conclusion Wheat OIT using wheat flour is safe and feasible with mild adverse reactions. Wheat OIT may be a promising therapy in children with IgE-mediated wheat allergy.

Key words wheat allergy, oral immunotherapy, food allergy, tolerance
Reference PR del Rio, et al. Oral immunotherapy in children with IgE-mediated wheat allergy: outcome and molecular changes. J Investig Allergol Clin Immunol. 2014;24(4):240-8.

Category: 1. Allergy 过敏
1381

Improvement of inattentive and hyperactive symptoms after treatment of rhinitis in school-aged children

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Abstract Content

Chronic rhinitis is a common problem in school-aged children. Treatment of rhinitis symptoms in children with AR could improve attention-deficit/hyperactivity symptoms.The current study aimed to evaluate inattentive and hyperactive symptoms changes after rhinitis treatment in children with chronic rhinitis.

Methods

Children age 5-18 years with chronic rhinitis were enrolled for a 3-month prospective study. Allergen sensitization was evaluated by skin prick test (SPT) and blood for Phadiatop. Rhintis children were classified into 2 groups: allergic rhinitis (AR) and non-allergic rhinitis (NAR) based on the evidence of allergen sensitization. Total nasal symptom score (TNSS) and inattentive and hyperactive symptoms using Vanderbilt ADHD Diagnostic Rating Scale (VADRS) assessed by parent and teacher were recored at baseline, 1, and 3 months after rhinitis treatment.

Results

Eighty-theree children were enrolled with the mean age of 9.12+2.85 years and 44.6% were male. TNSS and VADRS score decreased significantly after treatment. A greater baseline VADRS score was associated with substantial improvement of inattentive and hyperactive symptoms. Sixty-one children (73.49%) were AR and 22 children (26.5%) were NAR. There was no significant difference in baseline VADRS score between AR and NAR groups. In subgroup analysis, the significant decrease of VADRS score after 1 month and 3 months treatment were demonstrated only in the AR group ($p<0.001$). However, there was no significant change in the VADRS score in the NAR group.

Conclusion

Early treatmentfor rhinitis symptoms may benefit in the improvement of inattentive and hyperactive symptoms in school-aged children with rhinitis.

Key words Allergic rhinitis, ADHD, Inattentive and hyperactive symptoms, Non-allergic rhinitis

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Category: 1. Allergy 过敏
1509

Immunologic changes after dust mite rush subcutaneous immunotherapy in children

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Abstract Content Background: House dust mites (HDM) are the major causative allergen for allergic rhinitis. Allergen immunotherapy (AIT) is the only disease-modifying therapy for allergic rhinitis. Rush immunotherapy is the accelerated build-up schedules to reach the target maintenance dose.
Objective: To evaluate the kinetic changes of peripheral blood CD4+CD25+FOXP3+ regulatory T cells (Treg) and serum cytokines in children undergoing 2-day modified rush HDM AIT.

Methods Children aged 5-15 years with allergic rhinitis were enrolled for a 2-day modified rush HDM AIT. Peripheral blood CD4+CD25+FOXP3+ Treg, serum IL-4, IL-13, IFN- , and IL-10 were measured at baseline, finishing rush, achieving maintenance dose, 6 months, and 12 months after reaching maintenance dose. Specific IgE (sIgE) to HDM was evaluated at baseline and 12 months after getting maintenance dose. Rhinitis symptoms were assessed daily using a daily card.

Results A total of 12 children with a mean age of 13 years were enrolled. Rhinitis symptom-free days per month increased significantly after reaching the maintenance dose compared to baseline (from 9.5 days to 19.5 days, p=0.002), and the maximum improvement was seen at 1 year. The levels of Treg were significantly increased at 6 months after maintenance dose compared to baseline level (3.83+1.80% to 6.27+1.63%, $p < 0.001$). There were no significant changes in serum cytokines and sIgE to HDM after treatment. The systemic reaction during AIT occurred 7 episodes from 119 shots (5.9%).

Conclusion Two-day modified rush HDM AIT provides acceptable systemic reactions and increases the number of CD4+CD25+FOXP3+ Treg in children.

Key words Subcutaneous immunotherapy, Dust mite, Rhinitis, regulatory T cells, cytokines
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分类：1. Allergy 过敏
1511

Epidemiological characteristics and risk factors of obese asthma in school children aged 4-13 in Wuxi, China

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Background: Over the past few decades, the prevalence of both obesity and asthma in children has increased significantly in China. Accumulating studies have underlined the existence of an “obese asthma” phenotype as characterised by additional symptoms, worse control, and lower quality of life than other phenotypes. The first objective of this study was to investigate the prevalence of asthma and obesity of children in Wuxi area. The principle objective was to investigate the possible influencing factors of obese asthma.
Method: This was a city- wide, school-based cross-sectional survey in Wuxi, Jiangsu Province, China. The parents completed the questionnairy, including demographic questions and questions on a variety of birth, habit, and health topics. Data were collected from November 2018 to May 2019. In order to study variables as a predictive factor, logistic regression was used. The adjusted model was adjusted for the child’s sex and age, region of residence, parents' age, weight and education level, and family history of asthma. A $p < 0.05$ was considered significant.

Result: The prevalence of obese asthma was 1.23% of children aged 4 to 13 in Wuxi city. The risk of obese asthma in boys was significantly higher than that in girls (OR 2.05; 95%CI 1.38-3.04). Maternal BMI was associated with an increase in obese asthma (OR 1.04; 95% CI, 1.02-1.07) and paternal BMI was also associated with an increase in obese asthma (OR 1.06; 95% CI, 1.02-1.11), respectively. The risk of obese asthma in cesarean section infants increased by 2.15 (95%1.44-3.22) times. The risk of obese asthma in preterm infants increased by 2.16 (95%1.18-3.93) times. Compared with breastfeeding, the risk of obese asthma in children with formula and mixed feeding during 1st six months of life increased significantly (OR 1.94; 95%CI 1.10-3.42), (OR 1.69; 95%CI 1.12-2.55). Children with a family history of asthma had a higher risk of obese asthma (OR 2.39; 95%CI 1.60-3.56).

Conclusion: Our study indicates that obese asthma is related to gender, parents’ BMI, delivery type, gestational age, feeding mode, and family history of asthma. Evidence from this study highlights the effects of genetic and perinatal factors on childhood obese asthma.

关键字 children; obesity; asthma; risk factor; epidemiological characteristic

分类：1. Allergy 过敏
1537

Expression and clinical significance of IL-33 and its receptor ST2 in children with obstructive sleep apnea syndrome

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Abstract
Background: To detect the expression of interleukin-33 (IL-33) and its receptor ST2 in adenoids of children with obstructive sleep apnea syndrome (OSAS) as well as to explore the significance of IL-33/ST2 in the disorder.
Methods: 40 children undergoing adenoidectomy due to OSAS in the Otolaryngology of Tianjin Children's Hospital were selected as the study subjects. The number of IL-33 and ST2 positive cells in adenoids was detected by immunohistochemical SP method.
Results: IL-33 positive cells were mainly distributed in the submucosa epithelium and vascular endothelium, and expressed in the nucleus and cytoplasm. While ST2 positive cells were primarily observed in the mucosa and expressed in the nucleus and cytoplasm, a little expression of intercellular substance. There was a positive correlation between the proportion of adenoids in the posterior nostril diameter and the number of IL-33 positive cells. The expression of IL-33 in adenoids was positively correlated with the level of ST2 ($r = 0.809$, $P = 0.000$). The expression of IL-33 in adenoids was positively correlated with the level of eosinophil granulocyte ($r = 0.859$, $P = 0.000$). Moreover, the expression of ST2 in adenoids was positively correlated with the level of eosinophil granulocyte ($r = 0.814$, $P = 0.000$). The number of IL-33 positive cells was significantly higher in moderate hypoxemia group than that in mild hypoxemia group ($P < 0.05$). There was no significant difference in the number of ST2 positive cells between moderate hypoxemia group and mild hypoxemia group ($P > 0.05$).
Conclusions: Both IL-33 and its receptor ST2 were expressed in adenoids of OSAS children. The severity of airway obstruction caused by adenoid hypertrophy was positively correlated with the expression of IL-33.

关键字 Keywords: Children; obstructive sleep apnea syndrome; IL-33; ST2; adenoidal hypertrophy

分类：1. Allergy 过敏
1552

Mechanism of mixed probiotics relieving food allergy in infant mice through PD-1/PD-L1 pathway

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Objective To investigate the effects of mixed probiotics on food allergy and its mechanism. Methods BALB/c mice at 15 days of gestation were randomly classified into three groups: control group, food allergy group (OVA group) and mixed probiotics group. After birth, food allergy was established by OVA sensitization. The mixed probiotics group was given probiotics solution by gavage from day 21 to day 35 after birth. The control group received normal saline. 24 h after the last stimulation, intestinal histopathological sections were made to observe intestinal pathological changes, blood smears were prepared to count eosinophils, serum was separated to measure cytokines and OVA specific antibodies, and the content of DCs and Tregs in mesenteric lymph nodes was analyzed. Results Compared with OVA group, diarrhea score of mice treated with mixed probiotics decreased significantly, the concentration of IL-4, IL-5, IL-13, MCPT-1, and OVA specific antibody IgE and IgG in serum reduced significantly, the percentage of eosinophil decreased significantly. The concentration of IL-10 increased significantly. The level of PD-L1 on the surface of CD103+DCs and CD103+CD80-CD40-DC increased dramatically. The proportion of Tregs in CD4+T cells was significantly increased, and the level of PD-1 on the surface of Tregs was substantially increased ($P<0.01$). Conclusion Mixed probiotics can alleviate the symptoms of food allergy, reduce the level of inflammation, and the mechanism may be produced by the pd-1/pd-l1 pathway regulating Tregs, and the results provide new ideas for the diagnosis and treatment of food allergies.

关键字 Food Allergy; Probiotics; PD-1/PD-L1; Ovalbumin; Infant Mice

分类：1. Allergy 过敏
1651

Allergen analysis of 4622 children with allergic diseases in Shaanxi province

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Background: Allergic diseases are a class of diseases with tissue damage and/or organ dysfunction caused by abnormal immune response. Allergic diseases are complex and multifactorial. Environment plays a important role in the occurrence and development of allergic diseases. In recent years, some Chinese studies have summarized the allergens of allergic diseases in some areas, but there were few reports on allergens of allergic diseases in Shaanxi province. This study used the method of serum specific IgE antibody detection to analyze the allergen spectrum of children with allergic diseases in Shaanxi province, and analyzed the distributional characteristics of the allergens in different genders, ages, regions and seasons. Method: A total of 4622 children with allergic diseases diagnosed in the asthma outpatient in department of pediatric, Xijing hospital, from March 2015 to February 2019 were selected. Serum specific IgE of 19 allergens were detected by enzyme-linked immunosorbent assay. Children were divided into different groups according to the gender, age and region, and the distributional characteristics of allergens between different groups were compared. Results: The overall positive rate of 4622 children was 62. The highest positive rate was 24.2% of milk, followed by mold mix 18.0%, dog dander 16.7%, house dust mite 16.4%, cat dander 11.7%, cashew 10.7%, weed pollen 10.6%, egg white 8.8%, house dust 7.8%, tree pollen 7.7%, amaranth 5.6%, mulberry 4.9%, mango 3.6%, beef 3.2%, cockroach 2.8%, crab 2.1%, shrimp 1.5%, pineapple 0.8% and shellfish 0.3%. According to the analysis of gender, the positive rates of allergens in male were higher than that in female. According to the analysis of age, The positive rates of inhalation allergens increased and the positive rates of food allergens decreased with age. According to the regional analysis, The positive rate of house dust mite in the children patients in the Southern Shaanxi, the positive rate of weed pollen in the children patients in the Northern Shaanxi and the positive rates of milk and egg white of the children patients in the Guanzhong region were higher than that in other areas. According to the cluster analysis and correlation analysis, the 19 allergens could be roughly divided into 4 categories. There were moderate correlations among tree pollen, mulberry and amaranth. There were moderate correlations among mulberry, mango and amaranth. There was a moderate correlation between shrimp and crab, and there were mild or weak correlations among most of the other allergens. Conclusions: Among 4622 children with allergic diseases in Shaanxi Province who were treated in the asthma outpatient in department of pediatric, Xijing hospital, male children were more sensitive to allergens. The positive rates of inhalation allergens increased and the positive rates of food allergens decreased with age. There are regional differences in the distribution of allergens. Some allergens were correlated with each other, which may be related to cross-reaction.

关键字 Children; Allergic diseases; Allergen

分类：1. Allergy 过敏
1681

Safety of subcutaneous immunotherapy of dust mite in children with asthma and its relationship with clinical response

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Objective:

The safety data of subcutaneous immunotherapy (SCIT) of dust mite in children diagnosed asthma and the risk factors of adverse reactions were analyzed in our center, then the correlation between adverse reactions and clinical response was discussed, in order to provide a new clinical predictive indicator for the evaluation of SCIT efficacy.

Methods:

We enrolled 122 children, aged 6-16 years, with dust mite SCIT for more than one year.All the children were treated with the standardized dust mite SCIT regimen and outpatient follow-up regularly. The SCIT treatment record cards were complete and the clinical datas of 122 children were collected.

(1)The incidence, occurrence time, grade, and management of local reactions(LRs) and systemic reactions (SRs) were analyzed to evaluate the safety of SCIT in children with asthma.

(2)Separately counted the incidence of adverse reactions in each child to the needle times. Regarding the median as the critical value, the group less than the critical value was defined as the less adverse reactions group, greater or equal to the critical value defined as the multiple adverse reactions group.According to this standard,122 cases were divided into two groups. Use the single factor regression, then perform multivariate logistic regression analysis on the factors with statistical differences to obtain independent risk factors for adverse reactions.

(3) Lung function parameters and C-ACT scores were respectively compared before and after treatment in the less adverse reactions group and the multiple adverse reactions group to evaluate the improvement of lung function and asthma control level after SCIT.

(4) The differences in C-ACT score, total number of acute exacerbation, reduction in ICS and efficacy evaluation after treatment were compared between the two groups ,so as to evaluate the correlation between the incidence of adverse reactions and clinical efficacy.

Results:

1. Dust mite SCIT safety

(1)Among the 122 children, 5279 injections were received, and 608 LRs occurred, in a ratio of 11.52% per injection. All the LRs were mild to moderate degree.

(2)The SRs occurred 10 times, with a ratio of 0.19% per injection, including skin and lower respiratory symptoms. All the SRs were Grade 1 and Grade 2.

2. Risk factors of adverse reactions

Multivariate Logistic regression analysis showed that BMI (OR: 1.153;95% CI: 1.012 1.314;P= 0.033) or SPT result in Der f(OR: 2.106;95% CI: 1.377 3.221;P=0.001) was an independent risk factor for adverse reactions. Comparising OR values between the two groups,we found that SPT result in Der f was a more important risk factor than the other.

3. Safety and clinical response

(1)In the less adverse reactions group and the multiple adverse reactions group, pulmonary function indexes before and after SCIT in the two groups with safety differences were in the normal range, and there were no significant differences in FEV1%pred, PEF%pred, MMEF%pred and FeNO values.The C-ACT scores of children in both groups were significantly increased after SCIT(P=0.000), and the differences were statistically significant, suggesting that the asthma control level of children in both groups were improved after SCIT treatment.

(2)There were no significant differences in C-ACT score, total number of asthma acute excerbation in the past one year, reduction in ICS and SCIT efficacy evaluation between the two groups with safety differences after SCIT (P > 0.05).

Conclusions:

1. The dust mite SCIT in children with asthma has a good safety, with a low incidence of adverse reactions and mainly mild to moderate local reactions.
2. SPT result in Der f and BMI are independent risk factors for the occurrence of adverse reactions. The higher Der f SPT grade or BMI is , the greater possibility of adverse reactions in dust mite SCIT have.
3. The incidence of SCIT adverse reactions cannot predict the clinical response.

关键字 asthma; dust mite; subcutaneous immunotherapy; safety

分类：1. Allergy 过敏
1738

Compound impacts of climate change, urbanisation and biodiversity loss on allergic disease

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Background: Human activities have significant impacts on the environment, biosphere, and biodiversity. Due to the change in interactions between humans and the environment, several epidemics of allergic disease have emerged over the recent decades, particularly in childhood.
Objective: To review scientific evidence about compound impacts of climate change, urbanisation and biodiversity loss on childhood allergic disease.
Methods: A scoping review was conducted to examine independent and interactive effects of climate change, urbanisation and biodiversity loss on childhood allergic disease.
Results: Evidence suggests that environmental exposures rather than genetic factors are likely able to explain the increasing trend of childhood allergic diseases. Climate change, urbanisation and biodiversity loss impact aeroallergens such as pollen and fungal spores and allergic diseases such as asthma, allergic rhinitis and food allergy through complex interactions with multiple drivers.
Conclusions: Climate change, urbanisation and biodiversity loss have strong compound impacts on childhood allergic disease. It is imperative to understand the dynamic pattern of allergic diseases and develop effective strategies to prevent and control these diseases.

关键字 climate change，urbanisation，biodiversity loss，allergic disease

分类：1. Allergy 过敏
1793

The dysbacteriosis in pulmonary microbiota aggravates the inflammation of allergic respiratory diseases

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During the past few decades, the prevalence of allergic respiratory diseases in children, especially asthma caused by allergies, has been increasing year by year in China. Genetics, infection and endotoxin exposure, and intestinal microbiota are thought to be the main factors. Some changes in the pulmonary microbiota of asthma patients have been noted, when compared with that in normal people, opening the door to the concept that dysbacteriosis of pulmonary microbiome may play a role in the pathogenesis of chronic airway disease. However, the characteristics of the respiratory tract microbiome and its relationship with allergic disease in children are not clear. Whether there are specific bacterial colonies in the lungs of children with allergic respiratory diseases? Whether the intervention of bacterial microbiota can lead to changes in allergic inflammation? In previous study, we enrolled 68 children who underwent bronchoscopy from January 2018 to December 2018 in the affiliated hospital of the Capital Institute of Pediatrics. Using the total IgE (TIgE) values, children were divided into two groups: allergy sensitivity (AS) group and no allergy sensitivity (NAS) group. Nucleic acid was extracted from samples of bronchoalveolar lavage fluid (BALF) from the two groups of children taken during bronchoscopy treatment and the 16S rDNA gene was sequenced and analyzed. There was a statistically significant difference in the composition and distribution of microbiota between the AS and NAS groups ($p < 0.01$). Analysis of the correlation of clinical indices and microbiome showed that total IgE (TIgE) was positively correlated with Bacteroidetes and negatively correlated with Streptococcus. To verify the conclusion, we established the mouse model of the ovalbumin (OVA) induced asthma combined with the bacterial tracheal injection., and detected the indexes related to allergic inflammation in mice. The results showed the TIgE of mouse treated with OVA and Bacteroides fragilis, was higher than the mouse only treated with OVA solely. Consistently, the percentage of eosinophils increased, and the cytokines IFN-γ, IL-4, IL-5 in serum and alveolar lavage fluid increased significantly, comparing the mouse treated with OVA and Bacteroides fragilis with the mouse only treated with OVA solely. However, the TIgE did not increase in the mouse only treated with Bacteroides fragilis. Therefore, the dysbacteriosis in pulmonary microbiota may aggravate the inflammation of allergic respiratory diseases.

关键字 pulmonary microbiota, allergic respiratory diseases, TIgE, inflammation

分类：1. Allergy 过敏
1803

Skin prick test reactivity to House dust mites among allergic rhinitis or/and asthma children in Zhejiang

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Abstract

Objective: To investigate the sensitization of house dust mites (HDM) based on the results of skin prick test (SPT) among allergic rhinitis or/and children in Zhejiang Province.

Methods: We enrolled 230 patients between June 2017 to September 2019 in Zhejiang Province. Three groups of patients were recruited: allergic rhinitis (AR), allergic rhinitis and asthma (ARA), Asthma (A). SPT with HDM allergens, involving *Dermatophagoides pteronyssinus* (D.p) and *Dermatophagoides farina* (D.f) and Blomia tropicalis(B. tropicalis) was performed on 230 children. Positive outcomes were indicated in the degree of redness and swelling and the size of the wheal. According to the ratio of allergen diameter/histamine diameter (A/H) ratio, the skin index (SI) was divided into four levels. All patients were subjected to a HDM allergy questionnaire and measured serum IgE to HDM.

Results: 143 (62.2%) of 230 enrolled children were male, and 87 (37.8%) were female. 62.6% of the patients had at least 1 allergen positive using SPT. The prevalence of SPT reactivity was calculated in the population, with the following results: 59.6% for D.p, 58.7% for D.f,40.4% for B. tropicalis. There was significant difference of positive rate in HDM allergens between different disease groups. The positive rate of HDM allergens in ARA groups were higher than other groups (D.p：ARA:70.8%, AR 56.0%, A:45.8%; D.f：ARA:72.2%, AR 53.7%, A:45.8%, respectively), and the rate of positivity for D.p and D.f were significantly different ($p<0.05$). The positive rate of D,p and D.f in boy groups was higher than those in girls groups($P<0.01$,$P<0.05$),and the positive rate of B. tropicalis in adolescence was higher than those in childhood($P<0.01$).Furthermore, the most common SI of SPT positive results was level 4 (48.2%), the results indicated the number of level 4 of D.f and D.f in ARA group was significant higher than other two groups($P<0.05$,$P<0.01$).Bides, the positive of serum IgE to HDM (77.8%) was higher than SPT results(62.6%) and difference is statistically significant($P<0.001$).Meanwhile, the mean scores of the HDM questionnaire (9.46±6.17) and the skin index level had significant association ($r=0.393$, $P<0.001$). Children allergic to HDM in SPT were had higher scores to questionnaire($P<0.001$).

Conculsion: HDM was one the most important allergens of children with AR and/or asthma in Zhejiang. It also reveals the differences of SPT reactivity between different gender and ages of AR and/or children. Children with AR combined with asthma indicated higher sensitization of HDM allergens, which would be helpful for early tailored interventions.

关键字 Allergic rhinitis; Asthma; Children; Skin prick tests

Immunology

免疫

Category: 13. Immunology 免疫
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Clinical features and perforin A91V gene analysis in 31 macrophage activation syndrome with systemic onset juvenile idiopathic arthritis cases in China

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Abstract Content Objectives Macrophage activation syndrome (MAS) is a severe, potentially fatal complication of rheumatoid disease, especially in the systemic onset juvenile idiopathic arthritis (SoJIA). We investigated the clinical characteristics of 31 Chinese MAS cases with SoJIA and detected the perforin A91V gene in part cases.

Methods Methods Clinical characteristics of 31 SoJIA with MAS cases in the last nine years in our institute were retrospectively analyzed. Gene-specific polymerase chain reaction (PCR) primers were used to analyze the perforin A91Vgene polymorphism.

Results Results 31 SoJIA cases were associated with MAS. No specific medication was identified as trigger. 83% cases had infections prior to MAS. Clinical manifestations of MAS included persistent fever (100 %), hepatosplenomegaly (93.55%), lymphadenopathy (64.52%), and liver dysfunction (83.87%).Laboratory features included pancytopenia (41.9%),increased serum ferritin (87.10%), triglycerides (74.19%) and lactic dehydrogenase (87.10%). Hemophagocytosis were found in 27 cases (87.10%).The levels of NKcell in MAS patients was statistically below than the SoJIA and control group.The perforin A91V variant gene was detected in twenty cases ,but no mutation was found. Glucocorticoid,intravenous immunoglobulin，immunoimpressive therapy were effective. After treatment, 28cases (90.32%) were in remission, while 3 out of 31 cases died with a mortality of 9.68%.

Conclusion Conclusions MAS is a life-threatening complication of SoJIA. Most cases were preceded by infection. Unremitted fever, progressive hepatosplenomegaly, lymphadenopathy, cytopenias, elevated serum liver enzymes, significantly increased serum ferritin are the main feature. Prompt recognition and treatment is the key to improve prognosis. The perforin gene mutations in our patients have not found yet.

Key words Perforin, Systemic onset juvenile idiopathic arthritis, Macrophage activation syndrome, NK cells.

Reference

Category: 13. Immunology 免疫
55

The first report effective treatment of Tofacitinib in Chinese Pediatric patients with Blau syndrome

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Abstract Content Objective. Blau syndrome (BS) is a rare autosomal dominant, autoinflammatory syndrome characterized by the clinical triad of granulomatous recurrent uveitis, dermatitis and symmetric arthritis. associated with mutations in the nucleotide-binding oligomerization domain containing 2 (NOD2) gene. The aim of this study was to assess the efficacy of Tofacitinib in patients with BS.
Methods Methods. Tofacitinib was given to 3 patients with BS regularly, patient 1,2 and 3 received 1.7mg/day,2.5mg/day and 2.5mg/day. Patients' characteristics, clinical manifestations, magnetic resonance (MR) imaging, lab findings, and therapeutic measures were reviewed and treatment outcomes were described.

Results Results. three patients showed dramatic improvement of their clinical symptoms and laboratory findings. Three BS patients were all Chinese Han, and were men. three patients received tofacitinib, and all achieved clinical remission of polyarthritis rapidly, as well as normalization of erythrocyte sedimentation rate and C-reactive protein and improvements in inflammatory cytokines.

Conclusion Conclusion. JAK inhibitors such as Tofacitinib may be a promising approach for BS patients who have unsatisfactory response to corticosteroids, traditional disease-modifying antirheumatic drugs and biological agents

Key words Blau syndrome, NOD2, Tofacitinib
Reference

Category: 13. Immunology 免疫
59

Hemoperfusion and intravenous immunoglobulins for refractory gastrointestinal involvement in pediatric Henoch-Schönlein purpura: a single-center retrospective cohort study

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Abstract Content Immunoglobulin A vasculitis (IgA vasculitis [IgAV]), also called Henoch-Schönlein purpura, is a kind of common systemic vasculitis in children. Cases with refractory gastrointestinal (GI) symptoms is always difficult to handle because of its resistance to supportive therapies and glucocorticoid. This study sought to evaluate the efficacy of hemoperfusion(HP) and intravenous immunoglobulins(IVIG) therapies in this population.

Methods A single-center retrospective cohort study was conducted in 64 pediatric cases of HSP with refractory GI involvement (R-GI group) from March 2016 to October 2019 in Children's Hospital of Nanjing Medical University (Nanjing, China). The diagnostic criteria for HSP includes the presence of palpable purpura without thrombocytopenia or coagulopathy, with/without the following symptoms: i) arthritis/arthralgia; ii) Abdominal pain; iii) renal diseases. Refractory GI involvement was defined as the persistent GI symptoms that did not remit after 3 days of glucocorticoid treatment (prednisone 1-2 mg/kg/d orally, maximum dose of 60 to 80 mg per day or equivalent doses of parenteral dexamethasone) or dependent (relapsing twice when glucocorticoid was tapered). Among the R-GI cases, 42 patients (group A) received one dose of IVIG (2g/kg) combined with glucocorticoid (dose mentioned above), 13 patients (group B) were treated with HP every other day for 5-8 times as well as glucocorticoid, 9 patients (group C, resistant to IVIG or HP) were treated with a combination of IVIG and HP as well as steroid. To pair up, 64 cases with mild GI symptoms were included in the control case group from 1807 mild cases by randomized selection. Control cases received the symptomatic treatment or glucocorticoid (prednisone 1-2 mg/kg/d orally, maximum dose of 60 to 80 mg per day or equivalent doses of parenteral dexamethasone) to relieve the symptoms. The clinical features, baseline information, laboratory findings, treatment expenses, the length of hospitalization (LOH), and renal outcomes were collected. Laboratory results of pre-treatment were assessed at the time of diagnosis, and post-treatment indexes were collected after completing therapies and remission. All data were statistically analyzed by SPSS 25.0 software. P value < 0.05 was considered as statistical significance.

Results There were no significant differences between the control group and R-GI group in terms of age (7.09±2.77 years vs. 7.20±3.05 years, P=0.820), gender (male: 54.7% vs. 68.8%, P=0.103), body weight (26.53±11.13 kg vs. 26.90±13.42 kg, P=0.864). Before the treatment, patients in R-GI group tended to have higher level of white blood cell (WBC, P=0.000), neutrophils (Neut, P=0.000), C-reactive protein (CRP, P=0.004) and the percentage of B lymphocytes in the whole lymphocytes (BLY%, P=0.001) while the lower serum globulin (P=0.003), IgG (P=0.000) and IgM (P=0.000) compared with those in the control case group. Additionally, patients in the R-GI group were more susceptible with joint and renal involvement (53.13% vs. 25.00%, P=0.001 and

68.75% vs. 3.13%, P=0.000), more weight-corrected cumulative dose of steroid (47.15±16.71 vs. 19.09±9.60, P=0.000), and underwent 6 times expenses and 2.3 times LOH (All the P=0.000). The elevated Neut (P=0.000, OR=1.250) and BLY% (P=0.007, OR=1.100) as well as decreased IgG level (P=0.026, OR=0.847) were independent risk factors of refractory GI involvement in HSP. Elder HSP patients with GI bleeding were more susceptible to HSPN (P=0.014, OR=4.249). And in R-GI group, increased age (P=0.001, OR=1.039) and IgM (P=0.016, OR=5.994) were verified to be the independent risk factors for progressing to HSPN. Patients of group A were the youngest and had the lowest weight, experiencing the shortest hospital stay (P=0.016, 0.001, and 0.005, respectively), while there was no statistical difference of gender among three subgroups. Compared with group A, group B had the lower weight-corrected cumulative dose of steroid (P=0.033), and the medical expense of group A was approximately 1.5 times of group B (P=0.000). Although group B (HP therapy) had longer hospitalization than group A (IVIG therapy) (P=0.007), there's no relapse after HP therapy while 17.6% patients failed to achieve the remission after IVIG therapy. Both IVIG and HP therapy could efficiently induce the decrease of WBC counts (P<0.05), but the WBC and neutrophils count had the most decrease after HP therapy among three subgroups (P=0.039 and 0.003, respectively). While other indexes such as urinary RBC counts, urinary protein and BUN showed no significant differences between pre- and post-treatment. However, neither IVIG nor HP did not significantly influence the short-term and long-term renal outcomes.

Conclusion The HSP with refractory GI involvements was correlated with more steroid exposure, longer hospitalization, more medical expenses, and higher risk of renal disease, especially in those who were elder and/or had increased IgM level. Patients who accepted HP therapy tended to have less relapse, steroid exposure and medical expenses than those of IVIG therapy but the early start of either therapy did not influence the renal outcome. This study provides therapeutic options of refractory GI involvement in HSP as well as the evidence for identifying HSP patients with refractory GI involvement who were susceptible with poor renal outcomes.

Key words pediatric, Henoch-Schönlein purpura, refractory gastrointestinal symptoms, hemoperfusion, intravenous immunoglobulin G

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分类：13. Immunology 免疫
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Epidemiology, clinical characteristics, and prognostic factors of atopic children hospitalised for adenovirus infection

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Background: Atopy may be associated with the severity of disease and poor prognosis after adenovirus (Adv) infection in children. Our aim was to observe the clinical characteristics and pulmonary radiological changes in atopic children with Adv pneumonia in China.
Methods: Children hospitalised for Adv pneumonia from June 2018 to Dec 2019 were analysed. All children were divided into three groups: atopic with Adv, non-atopic with Adv, and atopic without Adv infection. Each group was further divided into mild or severe infection groups according to disease severity. Standard treatment was initiated after admission and regular follow-up evaluations were conducted at 1 month after discharge. Baseline and clinical characteristics, and pulmonary radiological changes of atopic and non-atopic children were collected. Risk factors associated with small airway diseases in Adv pneumonia patients were analyzed.
Results: Compared with non-atopic children with Adv infection, the cases of eosinophilic granulocyte count were significantly higher in atopic children than non-atopic children ($P<0.05$). Among children with mild and severe infection, the number of patients with wheezing and small airway disease as observed by high-resolution computed tomography (HRCT) was significantly higher in atopic children than non-atopic children ($P<0.05$). Furthermore, coughing was more severe in atopic children than non-atopic children ($P<0.05$). A family history of asthma (OR 2.1 [95% CI 1.8－3.0]), personal history of asthma (OR 2.7 [95% CI 2.1－3.1]), atopy (OR 2.1 [95% CI 1.8－3.2]), severe infection (OR 1.9 [95% CI 1.0－2.7]), and Adv infection (OR 1.4, [95% CI 0.9－2.0]) were independent factors associated with the development of small airway disease, both after admission and a month after discharge.
Conclusions: Atopic children with Adv infection experience more severe coughing during hospitalisation and are prone to wheezing and small airway disease on the HRCT. Family and personal history of asthma, atopy, severe infection, and Adv infection were independent factors associated with the development of small airway disease on the chest HRCT scan.

关键字 Adenoviral infection, Atopy, Children, small airway lesions

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Systematic analysis of the fluctuation of blood sirolimus concentration in children with CYP3A5 rs776746C/C genotype

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Objective: SRL (SRL) was mainly metabolized by CYP3A (Cytochrome P 4503A) enzyme and has large pharmacokinetic variability. This paper describes the clinical data of the drug in two children, initially analyzes the cause of blood drug concentration (TDM) fluctuations and its correlation with gene polymorphism.
Methods: The causes and clinical characteristics of the unexpected TDM concentration in 2 children with CYP3A5 rs 776746 CC genotype were analyzed and discussed together with the relevant literature.
Results: After unexpected TDM, the TDM reached 5-10ng/ml normal range. After detecting drug-related CYP3A genes, it was found that elevated TDM concentrations of SRL may be associated with the rs776746 C/C genotype. For A, drug interaction and metabolic genotype is the main cause of the significant increase in SRL blood concentration, combined drug effect on metabolic enzyme may continue, and stronger than metabolic genotype; For B, after doctors reduced the drug dose, the SRL blood drug concentration gradually returned to the target range, and the gene polymorphism may be the main cause of the abnormal increase in TDM.
Conclusion: When the unexpected TDM concentration is obtained, strict and systematic methods should be considered to analyze the cause, blood collection point, food factors, disease physiology, inter-drug interaction and gene polymorphism should be considered in the whole treatment cycle to reveal the cause and correct the treatment dose.

关键字 silomus; CYP3A5; drug gene testing; therapeutic drug monitoring（TDM）

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Eyelid Ptosis and Muscle Weakness in a Child with Kawasaki Disease: A Case Report

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Background Kawasaki disease (KD) is an acute febrile vasculitis that often occurs in children under 5 years. Ptosis and muscle weakness associated with KD are rarely documented. **Case presentation** We present a case of KD with eyelid ptosis and muscle weakness in a 3-year-old boy. At admission, laboratory evaluation showed hypokalemia with the serum potassium concentration of 2.62 mmol/L and hypoalbuminemia with the serum albumin concentration of 24.4 g/L. Intravenous immunoglobulin (IVIG) and aspirin were initiated immediately accompanied with methylprednisolone for adjunctive therapy. Potassium supplement and human albumin infusion were administered at the same time, which resulted in the correction of hypokalemia on the 2nd day of admission but no improvement in ptosis and muscle weakness. Neostigmine testing, lumber puncture, electromyography, and cerebral and full spine MRI were performed, which, however, did not find evidence for neural and muscle diseases. On the 5th day, the fever was resolved. On the 6th day, eyelid ptosis disappeared. And on the 14th day, the muscle strength and muscle tension returned to normal, patellar tendon reflex could be drawn out normally, and the boy regained full ambulatory ability. **Conclusions** KD might affect the neural and muscular systems, and KD complicated with eyelid ptosis and muscle weakness is responsive to the standard anti-inflammatory treatment plus adjunctive corticosteroid therapy.

关键字 Kawasaki disease; ptosis; muscle weakness; myositis; case report

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Clinicopathological analysis of 34 cases of primary Antineutrophil Cytoplasmic Antibody-Associated Vasculitis in Chinese children

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Background: This study aimed to summarize the clinicopathological features and prognostic risk factors of primary antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) in children.
Methods: Clinical and prognostic data for children admitted to our center with AAV between September 2003 and September 2020 were studied retrospectively. The incidence and risk factors of end-stage renal disease (ESRD) were calculated and analyzed.
Results: Thirty-four children were enrolled; 28 were female, with a median onset age of 10 years. Except for one case negative for ANCA, the other 33 patients were diagnosed with microscopic polyangiitis (MPA). The most frequently involved organ was the kidney (100.0%), followed by the lungs (58.8%) and heart (50.0%). Twenty children (58.8%) progressed to ESRD with a median course of 3 months, and they were more likely to present respiratory and cardiovascular system involvement than were the non-ESRD group ($P < 0.05$). Patients in the ESRD group also had a higher serum creatinine level, 24-h protein excretion, Pediatric Vasculitis Activity Score (PVAS), and a lower level of estimated glomerular filtration rate (eGFR), hemoglobin, and complement C3 than had those in the non-ESRD group ($P < 0.05$). The main pathological manifestations were crescentic and sclerotic classes in the ESRD group and focal class in the non-ESRD group. After 6 months of induction therapy, 90.0% of cases achieved complete or partial remission. The multivariate logistic regression model showed that baseline eGFR < 60 ml/min/1.73 m2 was an independent risk factor for progressing to ESRD (OR = 0.016, 95% CI = 0.001～0.412, P = 0.012).
Conclusions: AAV in children usually occurs in teenage girls, and the most commonly involved organ is the kidney, of which hematuria is the most common symptom, followed by proteinuria, abnormal renal function (eGFR < 90 ml/min/1.73 m2), etc. The primary type of AAV is MPA. Nearly 60% of patients progressed to ESRD with a median course of 3 months. Baseline eGFR < 60 ml/min/1.73 m2 is an independent risk factor for ESRD progression in AAV children.

关键字 antineutrophil cytoplasmic antibody-associated vasculitis,glomerulonephritis,pediatric patient

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Clinical study of systemic lupus erythematosus complicated with thrombotic microangiopathy in children

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Objective: To investigate the clinical characteristics, diagnosis, treatment and prognosis of systemic lupus erythematosus (SLE) complicated with thrombotic microangiopathy (TMA) in children.

Methods: The clinical data of patients with SLE related TMA treated in Beijing Children's Hospital from January 2015 to December 2020 were analyzed retrospectively, and their clinical characteristics, diagnosis, treatment and prognosis were studied.

Results: There were 8 patients with SLE related TMA, including 7 females and 1 male, with a median age of 12 years. Among them, 6 cases had TMA during SLE treatment, 1 case had TMA first, and other organ involvement 2 years later; SLEDAI scores were moderate to severe disease activity. 7 patients had hemolytic anemia, thrombocytopenia, nervous system damage, broken red blood cells in peripheral blood, 1 case had renal thrombotic microvascular disease, and 8 cases had renal damage; All 8 patients were treated with glucocorticoid combined with other medications, including 7 cases combined with immunosuppressant (cyclophosphamide or mycophenolate mofetil), 8 cases combined with intravenous immunoglobulin, and 1 case combined with rituximab; 5 cases were treated with plasma exchange. After treatment, one patient gave up due to aggravation of his condition; All 7 patients improved. All patients were accompanied by renal damage and increased D dimer.

Conclusion: Clinical manifestations combined with multiple blood smears are helpful to the early diagnosis of SLE related TMA. Patients with moderate and severe disease activity, renal damage and increased D dimer should pay attention to the risk of thrombotic microvascular disease. Early plasma exchange and glucocorticoid are important measures for successful treatment.

关键字 SLE, TMA, children

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Subcutaneous panniculitis-like T-cell lymphoma with hemophagocytic lymphohistiocytic syndrome in two children

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Background:
Subcutaneous panniculitis-like T-cell lymphoma is an uncommon form of cutaneous lymphoma in the pediatric population. It is characterized histologically by subcutaneous infiltration of pleomorphic cytotoxic T cells, mimicking a lobular panniculitis.

Method:
We present two pediatric patients with aggressive forms of subcutaneous panniculitis-like T-cell lymphoma complicated by hemophagocytic syndrome, and discuss the current literature.

Results :
Both cases are dignosed by gene reports,unfortunately their skin biopsies are negative.

Conclusions:
Although usually described as having an indolent clinical course, subcutaneous panniculitis-like T-cell lymphoma may be complicated by systemic involvement and hemophagocytic lymphohistiocytosis , resulting in a poorer prognosis.

关键字 panniculitis, Subcutaneous panniculitis-like T-cell lymphoma, hemophagocytic lymphohistiocytic syndrome,

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A novel CARMIL2 mutation in a child with dermatitis, chronic gastrointestinal eosinophilic inflammation and proteinuria

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Background Mutations of CARMIL2 are related to immunodeficiencies according to recent reports. CARMIL2 (RLTPR) gene encodes the capping protein regulator and myosin 1 linker2, which plays an important role in CD28 co-signalling as well as cytoskeletal organization of T cells. Therefore, mutations of CARMIL2 affects the normal function of human T-cell function. Method We show a novel mutation of CARMIL2 in a child with dermatitis, chronic gastrointestinal eosinophilic inflammation and proteinuria. Result An 11-year-old boy was hospitalized with repeated skin rash for 7 years and proteinuria for 3 months. He was born to healthy but consanguineous parents of Hui descent and presented initially at the age of 4 years old with symptoms of atopic dermatitis. The itching rash was located on the head and face at the beginning as well as swollen lips. The skin rash gradually turned into black plaques all over the body, and similar plaques were seen on the oral mucosa on both sides of the mouth. Blood routine: white blood cell (WBC) 10.3×109/L, absolute lymphocyte count (ALC) 4.86×109/L; urine routine revealed protein 2+, 24-hour urine protein 3.16g/24h, urinary microprotein suggested elevated albumin and slightly elevated transferrin (TRF), immunoglobulin G (IgG) and alpha-1-microglobulin (α1-MG), urine protein/urinary creatinine ratios: 2.60; normal serum albumin level and creatinine; negative Herpes simplex IgM, Cytomegalovirus IgM; positive mycoplasma IgM; EBV-antibody: IgM against the Epstein-Barr viral capsid antigen (EBCV-IgM) (-), IgG against the Epstein-Barr viral capsid antigen (EBCV-IgG) (+), IgG antibodies to EBV nuclear antigen (EBNA) (+); normal cerebrospinal fluid routine, biochemical and culture; ACTH>1250pg/ml with normal cortisol; negative ANA; lymphocyte subsets: low NK lymphocyte count and elevated T and B lymphocyte count; reduced Treg 3.3%; IgG subclass showed IgG2 level slightly elevated, and normal IgG1, IgG3, IgG4; Fluorescence staining of rash scrapes revealed a large number of fungal spores; normal cranial MRI. Abdominal skin biopsy: Epidermal focal keratosis, serous exudation and more neutrophils, spinous focal foveal edema, focal vacuolar degeneration of the basal layer, moderate lymphocytes and a small amount of neutrophils around the superficial small blood vessels of the dermis Cell infiltration. Gastrointestinal mucosa biopsy revealed that, antrum: Mild chronic inflammation of the mucosa, interstitial focal lymphocyte aggregation, eosinophil count 0～1/HPF; Descending duodenum: Mild to moderate chronic inflammation of the mucosa, eosinophil count 5～10/HPF; End ileum: Mild chronic inflammation of the mucosa, eosinophil count 3～5/HPF; Ascending colon: Moderate chronic inflammation of the mucosa, focal lamina propria formation, eosinophil count 5～10/HPF; Transverse colon: Mild chronic inflammation of the mucosa; Descending colon, sigmoid colon: Moderate chronic inflammation of the mucosa, mucosal lamina propria lymphocyte aggregation with lymphoid follicle formation, eosinophil count 20～30/HPF; Rectum: Mild to moderate chronic inflammation of the mucosa, interstitial focal lymphocyte aggregation, eosinophil count 20～30/HPF. Next-generation sequencing revealed that the child carries a novel homozygous mutation of CARMIL2 gene. Conclusion From literature review, we observed that the mutations of CARMIL2 found so far are all

homozygous mutations, and often involves the patient's skin, chronic inflammation of the digestive tract, and tumors. However, the boy in this report also had endocrine system, central nervous system symptoms and proteinuria.

关键字 CARMIL2; gastrointestinal eosinophilic; proteinuria

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Hepatic veno-occlusive disease with immunodeficiency (VODI): First reported case in China and literature review

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Objective: Hepatic veno-occlusive disease with immunodeficiency syndrome (VODI) was a rare form of combined immune deficiency (CID), which was characterized by hypogammaglobulinemia, combined T and B cell immunodeficiency along with veno-occlusive disease of the liver. VODI was an autosomal recessive immunodeficiency syndrome due to loss-of-function mutations in the SP110 gene. If VODI was not diagnosed timely and untreated with intravenous immunoglobulin and pneumocystis jerovici prophylaxis, the mortality is greater than 85%. So far, no confirmed VODI case has been reported in China.
Methods: The clinical data of the patient diagnosed with VODI in Beijing Children's Hospital were analyzed retrospectively, and the previously reported cases in the literatures were reviewed.
Results: A 7-year-old girl presented with recurrent pneumonia and otitis media since 2 years old. Her elder brother died from hepatic failure of undetermined etiology after birth with hepatosplenomegaly. Sputum culture suggested Streptococcus viridans infection, and feces PCR testing results was positive for enterovirus. Immunological evaluation revealed pan-hypogammaglobulinemia. Lymphocyte subset analysis showed decreased memory B cells but was otherwise unremarkable. Serum alanine aminotransferase level was elevated slightly. Results of liver ultrasound and enhanced CT scan of hepatic vascular were normal. Whole exome sequencing (WES) identified compound heterozygous mutations c.1342C>T (p.R448X), c.1342del (p.R448Efs*19) in SP110 gene. The patient received monthly infusions of intravenous immunoglobulin and pneumocystis jerovici prophylaxis since 5 years old, and the conditions improved. A total of 45 cases have been reported previously worldwide, males and females were almost equally presented. The median onset age was 3 months (range, 3 days to 3 years). Recurrent infections, failure to thrive, hepatosplenomegaly and ascites were the most common clinical manifestations. Pneumocystis infection was found in 15 cases. Laboratory studies revealed hypogammaglobulinemia presence in all patients with normal or decreased absolute counts of T and B lymphocytes. Most patients existed elevated liver transaminases. Veno-occlusive disease of the liver was revealed in more than half of the patients who received liver biopsy. Some children had no evidence of hepatic vein occlusion or appeared in the late stage of the disease. Most patients received antimicrobial prophylaxis and immunoglobulin replacement therapy. Eight children underwent hematopoietic stem cell transplantation and four cases received liver transplantation. Follow-up of 41 cases and in total 21 patients died. The median died age was 4.5 months (range, 2 months to 19 years).
Conclusion: This study reported for the first time VODI case in China to date and broadened the genetic spectrum of the disease. Recurrent infections, failure to thrive, hepatosplenomegaly and ascites were the most common clinical manifestations of VODI. Some children had no evidence of hepatic vein occlusion or appeared in the late stage of the disease. A high suspicion of VODI must be kept in mind for patients presenting CID early in life with deranged liver function or related family history. Hematopoietic stem cell transplantation is the definitive treatment. Regular

intravenous immunoglobulin and pneumocystis jerovici prophylaxis are effective supportive therapies.

关键字 Hepatic veno-occlusive disease; combined immune deficiency; SP110

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Streptococcal infection in childhood Henoch-Schönlein purpura correlation with renal pathology: a 5-year retrospective study

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Background: The present study focuses on the associations of streptococcal infection with the clinical phenotypes, relapse/recurrence and renal involvement in Henoch-Schönlein purpura (HSP) children.
Methods: 2074 Chinese children with HSP were recruited from January 2015 to December 2019. Patients' histories associated with HSP onset were obtained by interviews and questionnaires. Laboratory data of urine tests, blood sample and infectious agents were collected. Renal biopsy was performed by the percutaneous technique.
Results: (1) Streptococcal infection was identified in 393 (18.95%) HSP patients, and served as the most frequent infectious trigger. (2) Among the 393 cases with streptococcal infection, 43.00% of them had arthritis/arthralgia, 32.06% had abdominal pain and 29.26% had renal involvement. (3) 26.08% of HSP patients relapsed or recurred more than 1 time within a 5-year observational period, and the relapse/recurrence rate in streptococcal infectious group was subjected to a 0.40-fold decrease as compared with the non-infectious group. (4) No significant differences in renal pathological damage were identified among the streptococcal infectious group, the other infectious group and the non-infectious group.
Conclusions: Streptococcal infection is the most frequent trigger for childhood HSP and significantly decreases the relapse/recurrence of disease, whereas does not aggravate renal pathological damage.

关键字 arthritis; Henoch-Schönlein purpura; immunoglobulin A; renal pathology; streptococcus

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Vitronectin, a Novel Urinary Proteomic Biomarker, Promotes Cell pyroptosis in Juvenile Systemic Lupus Erythematosus

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Objective：To identify new markers of juvenile systemic lupus erythematosus (JSLE) that facilitate patient stratification and prognosis is quite important. The potential urine biomarkers of JSLE patients fit for the urgent demands in clinical diagnosis. Therefore, our aim of the present study is to analyze alteration of protein expression and potential valuable biomarkers in JSLE urine.

Methods：Based on this aim, proteomics assay analyzed the changes of urinary proteins among active JSLE patients (n=10), inactive JSLE patients (n=9) and healthy controls (n=9). The correlationship between clinical pathological parameters of JSLE patients and level of urinary VTN was qualified. The effect of VTN on cell pyroptosis was verified by the results of Western blot, qPCR and ELISA assay.

Results：Herein, we have identified a group of 105 differentially expressed proteins with ≥1.3 fold up-regulation or ≤0.77 fold down-regulation in JSLE patients. We found these proteins were involved in several important biological processes such as acute phase inflammatory responses, complement activation, hemostasis, and immune system regulation in gene ontology and functional enrichment analysis. Interestingly, we found and confirmed that urinary Ephrin type-A receptor 4 (EPHA4) and Vitronectin (VTN) were significantly reduced in both inactive and active JSLE patients. Moreover, VTN treatment in THP-1 derived macrophages significantly promoted the cell pyroptosis through the activation of inflammasome NLRP3. There is an activation of Caspase-1 and an upregulated secretion of cleaved GSDMD and IL-18 in VTN treated macrophages. Most importantly, the urinary VTN was also linear correlated with clinical characteristics of JSLE, implying VTN could be a specific diagnostic biomarker to distinguish inactive and active JSLE.

Conclusion：In summary, this study provided a urinary proteomic reference profile for JSLE to further assist clinical diagnose. Patients with active and inactive JSLE have differentially obvious metabolic proteins in the urine. VTN could be a specific diagnostic biomarker to distinguish inactive and active JSLE. This identified new biomarker supplied a new insight of larger prospective validation study in JSLE.

关键字 VTN, JSLE, Proteomics, Cell pyroptosis

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Enthesitis-related Arthritis (ERA): The Clinical Characteristics and Factors Related to Imaging Remission of Sacroiliitis

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Abstract
Objectives: To describe the clinical characteristics and explore the related factors of imaging remission of sacroiliitis in patients with enthesitis-related arthritis (ERA).

Methods: Patients with ERA at Xinhua Hospital affiliated with Shanghai Jiaotong University between 2018 and 2021 were retrospectively reviewed. Demographics, clinical characteristics, and treatments were described. Those with and without imaging remission of sacroiliitis were compared.

Results: In 146 patients with JIA, 94 ERA patients (53.2% male) were included. Median onset age was 10 years (IQR 7－11) and median disease duration was 12 months (IQR 5－21). Human Leukocyte Antigen (HLA)-B27 was positive in 27.7%. Acute uveitis occurred in 3.2%. Oligoarthritis was present in 81.9%. Hip, knee and ankle joints were among the most common joints involved. Enthesitis at diagnosis occurred in 29.8%, and sacroiliitis occurred in 78.7%. Methotrexate (MTX) remained the most common disease modifying anti-rheumatic drug (DMARDs) used (87.2%), and 56.4% were treated with biologics. Among 57 patients diagnosed with Sacroiliitis, 20 (35.1%) achieved imaging remission after treatment (follow-up time over 6 months). A shorter duration from onset to diagnosis (P=0.018), lower ESR (P=0.010) and without enthesitis (P=0.037) were associated with imaging remission of sacroiliitis.

Conclusion: ERA represented the most common category of JIA. Our study described clinical characteristics in ERA, and early diagnosis and treatment could improve the outcomes.

关键字 enthesitis-related arthritis, clinical characteristics, imaging remission, related factors

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Widespread usage of tocilizumab in COVID-19: a challenge from adults to children

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In the meta-analysis of Tleyjeh et al.,tocilizumab reduced the risk of mechanical ventilation in hospitalized patients with COVID-19,with no definitive evidence of a reduction in short-term mortality or an increased risk of infection.However limited information on the efficacy of tocilizumab in COVID-19 children has been summarized from systemic review.MIS-C is a life-threatening complication triggered by COVID-19,characterized by prominent cardiovascular involvement and excessive systemic inflammation with raised IL-6.IL-6 neutralization with tocilizumab may be an appealing therapy.Thus,scattered evidence implies somewhat conflicts on the efficacy and safety of tocilizumab in MIS-C.In this study,we preliminarily summarized the available studies on tocilizumab for MIS-C.

Studies were identified through searches of PubMed,Web of Science and Medline from inception to July 31, 2021.The search terms used were multisystem inflammatory syndrome in children OR MIS-C OR pediatric inflammatory multisystem syndrome OR PIMS AND tocilizumab.

A total of 6 eligible studies were identified including 36 MIS-C patients.Males outnumbered females(M/F ratio:1.1),with a median age of 11.1 years(range3-17).18.7% of patients were white,31.3% were black,50.0% were Hispanic.32.0% had KD-like features.Inflammatory mediators were significantly elevated with median CRP200mg/l,PCT30μg/l,SF712.5μg/l,IL-1>5000pg/ml,IL-6 303pg/ml.Apart from respiratory system,gastrointestinal tract was the commonest organ involvement,followed by cardiovascular,neurologic system.In patients with cardiovascular involvement,85.0% had shock,94.1% had elevated BNP,93.3% had elevated troponin.Echocardiograms were performed in 17 patients,of whom 11(64.7%) had a reduced LVEF(<50%),8(47.1%) had coronary artery dilation.After tocilizumab treatment,cardiac function significantly improved with increased LVEF(from 43.6% to 56.9%) and decreased BNP(from 2039.2pg/ml to198.1pg/ml).95.0% of patients were discharged alive with the median in-hospital duration of 5.9 days,1 patient(5.0%) died.

Although more than one third of MIS-C patients have KD-like features,60% of the patients would not have met criteria for KD.Epidemiologic studies of MIS-C have suggested that younger children are more likely to present with KD-like features,while children>5 years are more likely to develop cardiac dysfunction and even shock.Coronary artery dilation occurs in MIS-C patients regardless of KD-like features presented or not.We analyzed the data of 36 MIS-C patients with tocilizumab treatment,of whom,half were Hispanic with a median age of 11.1 years,68% were absent of KD-like features,47.1%-94.1% had cardiac dysfunction,85.0% underwent shock.Tocilizumab merits for those MIS-C patients who are Hispanic older children,absent of KD-like features,but in the presence of refractory cardiovascular dysfunction after initial treatments with IVIG/glucocorticoids.

In the study of Tleyjeh et al.,tocilizumab was not associated with an increased risk of secondary infections. Paradoxically,Somers et al. found that patients who received tocilizumab were more than twice as likely to develop a secondary infection than untreated controls(54%vs26%).The association between tocilizumab treatment and secondary infections is still controversial in adult patients with COVID-19,not to mention children in whom PID may be not rare.Shields et al. surveyed the outcomes of COVID-19 in 60 individuals with PID and suggested that the infection-fatality ratio,case-fatality ratio,inpatient mortality were estimated to be 20%,31.6%,37.5% in COVID-19 patients with PID,and 1%,1.5%,26% in COVID-19 patients without immunodeficiency respectively.We analyzed 6 eligible studies on tocilizumab for MIS-C,and found that secondary infections were elucidated by none of them.Further multicenter studies on comprehensive outcomes including secondary infections should be advocated in MIS-C receiving tocilizumab prior to widespread application in clinical practice.

关键字 COVID-19, tocilizumab, MIS-C

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Clinical heterogeneity of SCID with JAK3 deficiency

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Background: To summarize and analyze different clinical phenotypes of the combined severe immunodeficiency (SCID) due to JAK3 deficiency, in order to provide clues for early identification.

Method: The clinical manifestations and features of 2 children with JAK3 deficiency in our department were described and analyzed retrospectively.

Results:
A 3-month-old infant girl attended our hospital reporting "recurrent fever for 1 month". Fever occurred 1 month before admission without any symptoms. Detection of cellular and humoral immunity was performed for several times, the severe reduction in the proportion of T and NK cells was observed: CD3 T cells 2.0%, B cells 96.44%, NK cells 0.15%; Immunoglobulin levels are markedly decreased: IgA < 0.07 g/L, IgG 11.4 g/L and IgM 0.22 g / L; Infection was partially controlled with antibiotic therapy, but there was still intermittent fever.

Pregnancy and delivery history of mother: G1P1, female, 11 years old, suffering from congenital hip dislocation; G2P2, female, died from severe pneumonia at 6 months. The whole exon gene sequencing (WES) of second child showed JAK3 (chr19:17952197), c.1142 + 1G > A, diagnosed as immunodeficiency disease; Unfortunately, G3P3, as this child, was also diagnosed as JAK3 deficiency as the WES demonstration of pathogenic variant of JAK3 gene chr19:17952197, c.1142 + 1G> A (mother source); Chr19: 17951038, c.1254 + 1gG> t (father source).

During hospitalization, the infant suffered from recurrent high fever with rash, accompanied by signs of intracranial hypertension such as weakness, vomiting and fullness of anterior fontanelle. Laboratory investigations were as follows: Cerebrospinal fluid and peripheral blood NGS showed Mycobacterium bovis bacteria. Abdominal ultrasound displayed multiple infection foci in liver and spleen; Acid fast staining of bone marrow showed acid fast bacilli positive (1+): 3-9/100 visual fields. Considering the SCID background and history of BCG vaccination, the diagnosis of BCG disseminated infection was clear. Therapies include Isoniazid, rifampicin and meropenem, linezolid, voriconazole, amphotericin B as well as levofloxacin, but with poor response. On the 26th day after admission, the child experienced with seizure with oxygen desaturation and parents turn to treatment abandonment at last.

Another 9-year-old girl was admitted to our hospital with a 4-year history of verrucous papules on the nail margin. Four years ago, due to contact with grandma sufferd from "common warts", the girl developed cutaneous warts on both hands, with recurrence after intermittent finger tip cryotherapy. Laboratory tests showed a low

lymphcytes count to 0.6 × 10 ^ 9 / L, and a decreased proportion of CD3 T cells (43%), CD4 T cells (14%) and CD8 T cells (20%), a relative increased proportion of B cells (36%) and NK cells (18.5%). Gene sequencing showed that JAK3 deficiency c.2056G > A (p.D686N) (variant source father) and c.1205G > A (p.R402H) (variant source mother) which yielded Compound Heterozygous Mutations. The girl was diagnosed as combined immunodeficiency and started with compound sulfamethoxazole, imiquimod was used for enhancement of the local immune response. The girl was in regular follow-up now.

Conclusion: Mostly, JAK3 deficiency lead to SCID of T-B+NK- with early onset and severe infection, requiring hematopoietic stem cell transplantation; However, certain pathogenic variants of JAK3 gene can lead to a broad spectrum of clinical presentations, including milder immunodeficiency of later clinical onset. Therefore, patients who do not meet the typical phenotype of SCID may have variable JAK3 protein functions, and experiences on these rare individuals needs to be accumulated.

关键字 SCID JAK3 deficiency

分类：13. Immunology 免疫
1557

Analysis of the clinical manifestations of primary juvenile Sjogren's syndrome in a single center in China

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Objective: To analyze the clinical features of primary juvenile Sjogren's syndrome in China.
Methods: A retrospective cohort study included 41 children with primary Sjogren’s syndrome who were hospitalized in Peking Union Medical College Hospital from January 1, 2000 to December 31, 2020, with the age of onset younger than 18 years old. Onset manifestations, clinical manifestations and laboratory examination characteristics were summerized.
Results: Among the 41 cases of children, there were 10 boys and 31 girls. The minimum age of onset was 2.5 years, the median age of onset was 10.75 years, and the median age at diagnosis was 13 years. In terms of the onset presentions, fever or skin rash was observed in 12 (29%) and 9 (22%) children, respectively, while 5 (12%) children showed thrombocytopenia , and only 4 patients (10%) presented with typical symptoms of dry mouth and eyes. Besides, 3 children (7%) were firsted manifested with mumps. For overall clinical manifestations, referring to EULAR Sjogren's Syndrome Disease Activity Score (ESSDAI), abnormalities in constitutional domain, cutaneous domain, glandular domain, hematological domain, and biological domain are more common (41-70%) , while lymphadenopathy and lymphoma domain, articular domain, pulmonary domain, renal domain, and central nervous system domain may also occur (15-24%). No clear manifestations of musclar and peripheral nervous system domain were found in this cohort. Compared with the previous cohort, which are mainly western population, the proportion of fever, rash, pulmonary, renal and central nervous system involvement was significantly increased ($p<0.05$). In terms of oral examination, salivary gland ultrasound has the highest sensitivity (10/10, 100%), and the positive rates of parotid sialography and salivary flow rate are 89% (34/38) and 57% (21/37) respectively. For eye examinations, the tear film rupture test is more sensitive than the Schime's test as well as Rose bengal score. Compared with foreign cohort, the positive rate of salivary flow rate in Chinese children is lower, and the positive rate of corneal staining is higher ($p<0.05$). Other common laboratory abnormalities include elevated immunoglobulin, positive rheumatoid factor, abnormal thyroid function, and impaired renal tubular function.
Conclusion: The systemic clinical manifestations of juvenile primary Sjogren's syndrome are common while manifestations of gland involvement may not be obvious. And thus, it is strongly suggested to perform a detailed systematic assessments for patients with the possibility of primary juvenile Sjogren's syndrome.

关键字 原发干燥综合征；儿童；唾液腺超声

分类：13. Immunology 免疫
1558

A case of FOXN1 haploinsufficiency and literature review

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Objective To analyse the clinical and immunological characteristics of first case of FOXN1 haploinsufficiency in China and summarize the clinical characteristics of previous reported cases in other countries.

Methods The whole-exome sequencing(WES) and Sanger sequencing were conducted to verify the mutation of FOXN1.The TREC copies, peripheral blood lymphocyte subsets and TCR Vβ repertoire were further detected。A literature search was conducted using Wangfang Med Online, CNKI and PuMed with search terms “FOXN1 deficiency”,“FOXN1 haploinsufficiency”.

Results A 1-year-old girl manifested with recurrent autoimmune hemolytic anemia, hair loss and nail dystrophy. Her red blood cell count was 1.16×1012/L, hemoglobin was 45g/L, total bilirubin was 29.51umol/L, indirect bilirubin was 26.04umol/L, Coombs test was positive(++++), CD3+ T cells were 1284 counts/ul,CD4+ T cell were 195 counts/ul. Genetic mutation of FOXN1 (c.1392_1401delTCCTGGACCC,p.P465Rfs*82) was confirmed by WES and Sanger sequencing. The TREC was 0.35copies/ul. The TCR Vβ repertoire in this patient was markedly oligoclonal. Lymphocytes subsets revealed a predominate decrease of CD4+ T cell and NaïveCD4+T, an increase of effector memory helper T cells.A total of 5 publications were included(5 English and 0 Chinese).Thus far, 41 cases have been reported in the worldwide who mostly manifested with the decrease of T cells in early child. Clinical manifestations included repeated infection, hair loss, nail dystrophy, autoimmune disease and thymic dysplasia.

Conclusions FOXN1 haploinsufficiency deficiency is a kind of combined immunodeficiency disease, which is mainly manifested by the decrease of T cells and repeated infection in infants and young children, and may also accompanied by hair loss, nail dystrophy and autoimmune disease, which cannot be cured by hematopoietic stem cell transplantation.

关键字 FOXN1 mutation, Combined immunodeficiency

分类：13. Immunology 免疫
1691

The Current Status of Vaccination for Children with Rheumatic Diseases: A Single-Center Cross-Sectional Survey

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Background To understand the vaccination status of patients with rheumatic diseases registered at Children's Hospital of Chongqing Medical University, we deploy a cross-sectional questionnaire survey. **Method** An anonymous online questionnaire survey was distributed through www.wjx.cn. Consecutively inclusion of volunteer adults answered guardianship, guardians' education, residence, age and gender of children, diagnosis, treatment, as well as 19 questions about vaccine uptake, safety, and effectiveness, knowledge and attitudes towards vaccination. Survey data were collected from October 2020 to July 2021. Data were managed in Microsoft Excel and univariate and multivariate analysis were performed using IBM SPSS Statistics, version 26. A P-value ≤0.05 was considered statistically significant. **Results** A total of 171 adults responded to the investigation. 74.3%(127/171) were mothers, 51.5%(88/171) were residents in Chongqing province. 116 of 171 participants provided education, among which 39.7%(46/116) graduated from junior high school. All children include 50.9%(87/171) males and 49.1%(84/171) females, in which 32.7%(56/171) were juvenile idiopathic arthritis, 18.1%(31/171) were systemic lupus erythematosus, 18.1%(31/171) were Kawasaki disease, 14.0%(24/171) were Henoch-Schonlein purpura, 11.1%(19/171) were juvenile dermatomyositis, and 5.8%(10/171) were other diseases. The patients enrolled in our study had a mean age of 106.3 months and 62.6% were more than 7 years old. Age-appropriate vaccine completion: 66.1%(113/171) completed age-appropriate vaccination. The parents' worry or hesitation was identified as a factor affecting the completion results (P<0.05). There were no statistically significant differences in the completion of age-appropriate vaccination among different genders, ages, diseases, guardianship, residence, attitudes towards the necessity of vaccination, and the reasons for not completing vaccination. Treatment and Vaccination: The percentages of glucocorticoids, traditional disease-modifying anti-rheumatic drugs, biologics, intravenous immunoglobulin, and other symptomatic treatment were 64.3%(110/308), 53.8%(92/308), 33.9%(58/308), 25.7%(44/308), and 2.3%(4/308), respectively. 66.1%(113/171) were vaccinated as scheduled, and 5.3% (6/113) were only vaccinated with inactivated vaccine during treatment; 33.9%(58/171) were not vaccinated as planned, and 5.2%(3/58) had only received inactivated vaccine during treatment. There was a significant difference (P<0.05) between varicella vaccination or not on the occurrence of varicella during treatment. Factors affecting vaccination: Iatrogenic factors, as one of the three major factors for failing to complete vaccination, accounted for 66.1%(38/74), of which 27.6%(16/74) were due to doctors' recommendation and 37.9%(22/74) were due to advice from vaccination related staff. 29.3%(17/74) were attributed to parents, mainly because parents gave up to vaccinate

due to their worries and sometimes missed it. Other factors accounted for 32.8%, but the parents did not explain the exact reason. **Conclusions** At present, the completion rate of vaccination for RD children is not high. Suggestions from doctors or vaccination department staff, reasons from parents to fail to vaccinate, and other unknown factors mainly affect vaccination rate. The proportion of children vaccinated with inactivated or attenuated live vaccines during treatment was not high. The percentage of children infected with varicella during treatment who did not receive varicella vaccine was more than that of those who received varicella vaccine. Therefore, it is still essential to strengthen the prevention of common infectious diseases, vaccination education to increase awareness of medical and vaccination-related personnel, parents, and others on the vaccination regulations, and improve the vaccination rate of children with RD.

关键字 rheumatic disease, children, vaccination

分类：13. Immunology 免疫
1703

WASP is essential for maintaining regulatory T cells tolerance by inhibiting IL-2 receptors internalization and degradation

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Background：The Wiskott-Aldrich syndrome (WAS) occurs in males with hemizygous mutations in the X-chromosomal WAS gene. About 42-70% of Wiskott-Aldrich syndrome (WAS) patients suffer from autoimmune diseases, which are the most severe complications. WASP is an actin regulator, which affect multiple immune cells. We found the suppressive function of WASP-/- regulatory T cells were impaired, which might cause autoimmunity. Regulatory T cells (Treg) play an important role in maintaining peripheral tolerance. Distinct molecules and pathways impact the ability of Treg cells, and are presumably amenable to therapeutic manipulation. However, the mechanism how WASP regulates Treg cells remains elusive.
Methods: We analyzed the Treg subsets of WAS patients and WASP knockout mice by Flow cytometry. We stimulated WT and WASP deficient naive CD4+T cells with anti-CD3/CD28 beads, and co-cultured with different percentage of WT and WASP-/- Treg cells respectively. To figure out whether enhancement of IL2-IL-2R signaling could increase the absolute numbers and the suppressive function of WASP-/-Tregs in vitro and in vivo, we added extra IL-2, JES6-1 mAb in suppressive assay and by abdomen injection in vivo, respectively. The absolute numbers were tested by Flow. Meanwhile, the levels of active markers PD-1, ICOS and CD103, inhibitory markers GITR, CTLA4 and LAG3 were analyzed by Flow. To see the signaling consequence of WASP-/- Tregs, we quantified STAT5, PI3K-MTOR，MAPK-ERK phosphorylation by western Blot and Flow. To examine the mechanisms on WASP deficiency downregulated IL-2 －IL-2R signaling, we quantified IL-2 receptors internalization triggered by IL-2 through FLOW. To investigate the trajectory of IL-2 receptors after internalization, we analyzed the colocalization of IL-2 receptors with endosome and lysosome markers EEA1, Lamp-1, Rab7, Rab11 by confocal. We quantified the recruitment of p-NWASP and dynamin on lipid by layers by TIRF microscopy. We did RNA sequence to screen the transcriptional files of the IL-2-IL-2R pathways.
Results: We found that thymic and peripheral Treg cells were significantly reduced in mice. The levels of resting Tregs, effector Tregs, central memory and effector memory Tregs were decreased both in knockout mice and WAS patients. Meanwhile, the active markers of PD-1, ICOS and CD103, the inhibitory markers of GITR, CTLA4 and LAG3 were decreased in WASP-/-Tregs. Suppressive assay showed WASP-/-Tregs could not inhibit WASP-/- Teff, which were consistent with previous data. We found the absolute numbers of Tregs were increased and the suppressive functions were enhanced in WASP-/-Treg cells after treated with IL-2 with JES6-1 mAb in vivo and vitro. And colitis were alleviated at day 5. As N-WASP phosphorylation and dynamin could increase IL-2 receptors internalization, we found that IL-2 receptors were internalized more in WASP-/-Treg cells than WT Treg cells by Flow. We also found the recruitment of p-NWASP and dynamin were more and earlier by TIRF. What’s more, we found the levels of STAT5, PI3K-MTOR and MAPK-ERK phosphorylation were decreased. To explain the signaling consequence, we found the co-localization of IL-2 receptors with Lamp1(endosome marker) were better in WASP-/-Treg cells，and the RNA sequence showed

the levels of transcriptional genes associated with endosome were increased in WASP-/-Treg cells, which demonstrated that IL-2 receptors might be degraded in endosome. Conclusion: This study demonstrated the mechanism on WASP deficiency increased IL-2 receptors internalization and degradation in endosome, which lead to decreased IL-2-IL-2R signaling. This study was the first demonstration of actin regulator protein WASP was essential for maintaining Treg cells
tolerance by affecting IL-2-IL-2R signaling trafficking. As a consequence, it provides insights on developing new therapeutic methods for WAS patients and other autoimmune disease in the future.

关键字 Wiskott-Aldrich syndrome ; autoimmunity; Regulatory T cells; IL-2-IL-2R internaliztion and degradation;

分类：13. Immunology 免疫
1704

Clinical characteristics of Behcet's syndrome in children

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Abstract: Objective to explore the clinical characteristics of Behcet's syndrome (BS) in children and to provide references for the establishment of domestic classification criteria and treatment guidelines for BS in children.
Methods: The clinical data of children who met the diagnostic criteria of BS in our hospital from January 2009 to June 2021 were analyzed retrospectively. The clinical manifestations, laboratory examination and treatment methods were summarized.
Results:1. General condition: among the 28 patients, there were 18 males and 10 females, with a male-to-female ratio of 1.8 to 1. The age of onset ranged from 6months and 20 days to 13 years and 4months, with an average age of 6.0 ±4.1 years. The age of diagnosis ranged from 7 months to 14 years, with an average age of 8.5 ±4.2 years. The course from diagnosis to onset ranged from 10 days to 12 years, with a median course of 1.8 years. 6 cases (21.4%) had family history of related diseases, 5 cases had adenoidectomy, circumcision and appendicitis, 2 cases had malnutrition, 1 case had dwarfism and 1 case had severe osteoporosis. 2. The first symptoms: the most common clinical manifestations oral aphthous ulcers (21 cases, 75.0%), followed by fever (5 cases, 17.9%), digestive system involvement (4 cases, 14.3%), joint involvement and eye involvement (2 cases each, 7.1%), skin lesions, genital ulcers and perianal ulcers (1 case, 3.6% each). 3. Clinical features: all children had recurrent oral aphthous ulcers (28 cases, 100%), digestive system manifestations, genital / perianal ulcers in 19 cases (67.9%), skin lesions and joint involvement in 11 cases (39.3%), eye involvement in 9 cases (32.1%), nervous system manifestations in 6 cases (21.4%), vascular involvement in 5 cases (17.9%). 4. Laboratory investigations, endoscopic and pathological findings: 11 cases (61.1%) had positive findings in gastroenteroscopy, mainly characterized by ulcers scattered in the colon and rectum, as well as intestinal stricture, esophageal or perianal ulcers; pathology was dominated by lymphocyte and neutrophil infiltration. In the laboratory examination, 4 cases (14.3%) showed increase of white blood cell count, mainly neutrophils, 11 cases (39.3%) had decreased hemoglobin, more than half of ESR and CRP increased, 3 cases IgA increased, 5 cases IgM increased, 7 cases IgE increased, 5 cases (18.5%) of ANA antibody were positive, and 1 case (3.7%) was anti-Jo-1. One case of TNFAIP3 gene missense mutation in exon 6 c.1804A>T (p.T602S) was found by gene detection, which was diagnosed as Haploinsufficiency of A20 (HA20). The brother with recurrent oral ulcer had the same heterozygous mutation. 5.Treatment and prognosis: 22 cases were treated with corticosteroids, of which 7 cases were treated with methylprednisolone(1mg/kg) intravenous drip, some of them were treated with immunosuppressants (cyclosporine A, methotrexate), 5 cases were treated with local drugs, and 9 cases were treated with biological agents (infliximab and Tocilizumab). The symptoms and inflammatory indexes were well controlled and the amount of corticosteroids decreased gradually.
Conclusion: Mucosal lesion is the main manifestation of pediatric BS in China, and the gastrointestinal manifestations and eye symptoms are severe. The current diagnostic criteria are not sensitive to the diagnosis of pediatric BS in Chinese. Children with younger age of onset, family history and severe symptoms should consider gene detection and identify Behcet-like inflammatory diseases such as HA20.

Biological agents have been initially used in the treatment of BS in children, but large sample studies are still needed to evaluate their safety and efficacy.

关键字 Behçet’s syndrome,Children,Haploinsufficiency of A20

分类：13. Immunology 免疫
1712

A case with good response to belimumab for pediatric IgG4-related disease

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IgG4-related disease (IgG4-RD) is an immune-mediated fibro-inflammatory disorder,which occurs in middle aged men, rare in children.In the case reports about pediatric IgG4-RD,the median age of the children was 13 years, of which 64% were girls.IgG4-related orbital disease (44%) and autoimmune pancreatitis type 1/IgG4-related pancreatitis (12%) predominantly occurred.Less frequently, other manifestations as pulmonary manifestation, cholangitis and lymphadenopathy were also found. The pathogenesis of IgG4-RD remains incompletely defined.We report the case of a 11-year-old female child who presented with recurrent oral ulcers,Sublingual excrescence and submandibular gland enlargement.Histopathological findings of the left cheek mucosa revealed a lymphoplasmacytic infiltrate,IgG4 positivity and IgG4+:IgG+ plasma cell ratio of >40%.Finally, IgG4-related disease was diagnosed after excluding other diseases.After treatment with belimumab combined with Prednisone and Cyclophosphamide, serum concentration of IgG4 fell to normal.The oral ulcers resolved completely without further outbreaks and submandibular gland enlargement was improved.The dose of glucocorticoid was tapered. This appears to represent the first case of a pediatric patient with oral ulcers as the first symptom, and also the first report of a case in which IgG4-RD was effectively treated using belimumab. This case provides a reference that belimumab may be a good option for maintaining treatment for IgG4-RD.

关键字 Belimumab;IgG4-related disease;child

分类：13. Immunology 免疫
1713

Deficiency of adenosine deaminase in children: the first case series from China

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Background: Adenosine deaminase (ADA) is a key enzyme for the purine salvage pathways. Genetic defects of ADA gene cause a subtype of severe combined immunodeficiency (SCID), known as ADA-SCID, accounting for about 10-15% of all SCID. Few Chinese cases have been reported. This study is the first case series from China describing the clinical and genetic characteristics of children with ADA deficiency.
Methods: We retrospectively reviewed the medical records of 3 patients diagnosed with ADA deficiency in Beijing Children's Hospital and summarized the previously published ADA cases from China in literatures.
Results: Eight children from China with ADA deficiency were included. Three were identified at Beijing Children's Hospital and five reported previously in the literatures from 1989 to 2020. The 8 patients were from 6 unrelated nonconsanguineous families. Half of the patients was onset after birth and the latest time of onset was 1 year-old. Respiratory tract infection and opportunistic infections were shown in 7 of 8 cases respectively. And 5 of 8 cases failed to thrive. Five of 8 cases showed reduced or absence of thymus by CT scan or chest X ray. P6 had language and fine motor degeneration. The visions of both eyes was blurred at the third year after diagnosis. The cerebral aneurysm was diagnosed in P6 by cranial angiography. Homozygous or compound heterozygous mutation of ADA gene were identified in six patients, including two nonsense mutations and four missense mutations. Two mutations were newly defined. Two patients were diagnosed based on clinical manifestations and ADA enzyme activity. Laboratory studies revealed cellular and humoral immune deficiency (T-B-) in all patients, and neutropenia was indicated 4 cases. ADA activity was examined in 5 patients, and the results were all reduced (4 cases in serum and 1 case in erythrocytes). Antibiotic prophylaxis as well as intravenous immunoglobulin were all accepted except for P1. In total 5 patients died and the median died age was 4 months (range, 29 days to 10 months). P2 had ERT and the immune function was partially reconstructed after 1 month follow-up. Delay-onset P6 was generally stable, HSCT was prepared and surgical treatment was planned.
Conclusions: This study described the first case series of Chinese ADA deficiency patients to date. In this series we identified six mutations in ADA deficiency and two mutations were new. Consistent with previous literatures, early-onset infection, failure to thrive and thymus abnormality were the most common manifestations of ADA-SCID. In addition, we reported cerebral aneurysm for the first time in ADA deficiency. The impaired purine metabolism and accumulation of substrates may contribute, at least partially, to the development of cerebral aneurysm, as they played an important role in vascular inflammation. Further study was warranted to investigate the underlying mechanisms.

关键字 Deficiency of adenosine deaminase, Severe combined immunodeficiency, Children, China

分类：13. Immunology 免疫
1718

Tofacitinib versus methotrexate in juvenile dermatomyositis: short-term results from a prospective observational cohort study

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Background: Juvenile dermatomyositis (JDM) is an autoimmune disease associated with type I interferon. Tofacitinib (TOF) inhibits pathogenic type I interferon signaling, but its use in juvenile dermatomyositis lacks high-quality clinical evidence and positive control studies.
Patients and methods: We conducted an open-label prospective observational cohort study in newly treated and relapsed children with JDM. All patients and their legal guardians were free to choose glucocorticoid plus tofacitinib or glucocorticoid plus methotrexate (MTX).
Result: 13 patients were in the MTX group and 12 patients in the TOF group. The two groups did not differ significantly in the proportion of responses as assessed by PRINTO 20 criteria and 2016 clinical response criteria at 6 months. The median time to rash clearance was 13 months in the TOF group but not observed in the MTX group (7.54-fold [95% CI 1.7－33.5] increase with prednisone plus tofacitinib; p=0・021). Treatment with tofacitinib resulted in improvements in FVC, PEF, VC and TLC of lung function. We found a significant decrease of interferon stimulating gene (ISG) expression after treatment with tofacitinib. Both the ISG sum score and median fold were positively correlated with the disease activity score (DAS). The frequency of adverse events did not increase in the TOF group.
Conclusion: Tofacitinib may not be inferior to methotrexate in terms of response rates in children with newly treated and relapsed JDM. Tofacitinib showed better results in rash healing and improvement in lung function. Detection of ISG levels helps to evaluate disease activity.

关键字 Juvenile dermatomyositis, type I interferon, JAK inhibitor, interferon stimulating gene, cohort study.

分类：13. Immunology 免疫
1725

Clinical characteristics of Kawasaki disease during the epidemic period of COVID-19 in Chongqing

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【Abstract】:Objective To analyze the clinical characteristics of Kawasaki disease (KD) during the epidemic period of Coronavirus disease 2019(COVID-19), and to establish a prediction model of intravenous immunoglobulin (IVIG) unresponsive KD based on discriminant analysis. Methods A total of 765 children with KD diagnosed in the affiliated Children's Hospital of Chongqing Medical University from January 2019 to December 2020 were selected and divided into two groups according to the time of visit: "before COVID-19 epidemic" group (2019.01.01-2019.12.31) and "during COVID-19 epidemic " group (2020.01.01-2020.12.31). The medical records of the two groups were collected and the differences between the two groups were compared.Then the statistical method is used to select indicators to establish an IVIG non-response prediction model based on discriminant analysis (SDA). Results During the epidemic period of COVID-19, the hospitalization time of the children in the group was longer and the proportion of infants was higher. The number and trend of visits in each month were different between the two groups ($P < 0.05$). During the epidemic period of COVID-19, the incidence of sepsis (8.3%), nervous system involvement rate (7.2%), BNP and ALT levels were higher than those in "before COVID-19 epidemic" group, while pneumonia (18.4%), diarrhea (31.6%), ESR and LDH levels were lower than those in "before COVID-19 epidemic" group ($P < 0.05$). The pathogen infection rate in the “during COVID-19 epidemic” group (33.9%) was significantly lower than that in "before COVID-19 epidemic" group (42.2%), and the difference was statistically significant ($P < 0.05$). Color Doppler echocardiography showed that during the epidemic period of COVID-19, the degree of coronary artery damage (CAL) was more severe, and the non-response rate of IVIG (12.6%) and hormone utilization rate (6.9%) were higher ($P < 0.05$). The duration of fever, WBC, N%, PCT, PT, the incidence of CAL and the proportion of incomplete KD in the IVIG non-reaction group were significantly higher than those in the IVIG reaction group, while the ALB was significantly lower than that in the IVIG reaction group. The function of the IVIG non-response prediction model established by Fisher discriminant analysis is as follows:
$Y0=-126.441+2.458X1+2.277X2+7.267X3+0.368X4+26.602X5-0.087X6+8.847X7+5.208X8$, $Y1=-118.783+1.929X1+2.350X2+6.508X3+0.333X4+23.321X5-0.149X6+8.628X7+5.791X8$ (where Y0 is IVIG reaction type, Y1 is IVIG non-reaction type; X1 is fever days, X2 is ALB, X3 is CAL, X4 is WBC, X5 is N%, X6 is PCT, X7 is PT, X8 is complete KD. The correct rate of model discrimination is 85%. Conclusion The epidemic prevention measures under the epidemic situation of COVID-19 effectively reduced the transmission of pathogens and changed the seasonal epidemic characteristics of KD, but the proportion of small infants increased, CAL was more serious and the incidence of IVIG resistance was higher. The risk factors of non-response to IVIG included long duration of fever, high levels of WBC、N%、PCT and PT, CAL and incomplete KD.

关键字 Kawasaki disease;Clinical features; intravenous immunoglobulin; non-response; discrimininant analysis

分类：13. Immunology 免疫
1733

A case report of ataxia telangiectasia with hypertension as a prominent manifestation and literature review

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Objective: Ataxia telangiectasia (AT) is a rare autosomal recessive primary immunodeficiency disease. ATM, the causative gene is located on chromosome 11q22.3. Most of the mutations are compound heterozygous mutations. The clinical manifestations of the disease are different, mainly manifested as cerebellar ataxia, immunodeficiency, growth retardation, extreme sensitivity to ionizing radiation and tumor, of which cerebellar ataxia is the main clinical manifestation. In this paper, we report a child with recurrent pulmonary infection and hypertension as prominent manifestations, whose neurological symptoms were not obvious, and who also had hypertension, in order to further improve clinicians' understanding of the disease.
Methods: The clinical data of a child with AT were collected and analyzed by whole exome sequencing using high-throughput second-generation sequencing technology, gene data analysis and suspected pathogenic mutation verification (using Sanger sequencing technology) to further confirm the diagnosis.
Results: The main manifestations were recurrent pulmonary infection, cheek and conjunctival telangiectasia, elevated IgM, elevated IgM, decreased IgG and IgA, and elevated serum alpha-fetoprotein. The clinical manifestations and laboratory examinations were consistent with the disease. Whole-exome sequencing analysis was performed using second-generation sequencing, and the results showed two heterozygous mutations in the ATM gene in the proband, c.468G > A (exon5, p.W156X) and c.5644C > T (exon37, p.R1882X), all nonsense mutations. After pedigree verification, the father of the proband with c.468G > A (p.W156X) had a heterozygous variant at this locus, which was normal in the proband's mother; the mother of the proband with c.5644C > T (p.R1882X) had a heterozygous variant at this locus, which was normal in the proband's father, consistent with autosomal recessive disease pathogenesis.
Conclusion: The possibility of AT should be considered in children with recurrent infection, cerebellar ataxia and telangiectasia of skin and conjunctiva, elevated immunoglobulin IgM and serum alpha-fetoprotein. In this case, the child had no obvious central nervous system abnormalities, and in addition to recurrent pulmonary infections, there was recalcitrant hypertension, which may be a new clinical phenotype of ataxic telangiectasia.

关键字 儿童，毛细血管扩张，共济失调，高血压

分类：13. Immunology 免疫
1749

Mimickers of Juvenile Idiopathic Arthritis

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Objective: To explore the disease that is easy to be misdiagnosed as juvenile idiopathic arthritis due to joint symptoms, in order to improve the vigilance of clinicians.
Methods: 13 cases of non juvenile idiopathic arthritis diagnosed in our hospital were reviewed to share the experience of diagnosis.
Results: Case 1: Guo * *, male, 15 years old, the chief complaint was "intermittent multi joint pain 4 months" , Ultimately diagnosis was tuberculous arthritis; Case 2: Feng * *, female, 8 years old, the chief complaint was "intermittent fever and multi joint pain for 25 days". Finally the child was diagnosed acute lymphoblastic leukemia; Case 3: Wen * *, female, 10 years old, the chief complaint was "fever and joint pain 2 months". Iliac bone biopsy showed Langerhans cell histiocytosis which was the finally diagnosis; Case 4: Zhang * *, male, 10 years old, the chief complaint was "swelling and pain of knees for 5 months and lumbosacral pain for 3 months". Synovial pathology suggested pigmented villonodular synovitis which was the final diagnosis; Case 5: He * *, male, 9 months old, the chief complaint was "swelling of the right knee for one month". The boy was finally diagnosed as hemophilia A; Case 6: Wang * *, male, 8 years old, the chief complaint was "intermittent stiffness of both lower limbs for 2 years, intermittent pain of the left lower limb with claudication for 3 months". The final diagnosis was spinal epiphyseal dysplasia (Schwartz Jampel syndrome type I) ; Case 7: Zhang * *, female, 11 years old, the chief complaint was "limited joints activity of both hands for 3 years and claudication for 9 months". The basic reason suggested that GNPTAB gene mutation, and the patient was finally diagnosed myxolipid storage disease; Case 8: Guo * *, male, 7 years old, the chief complaint was "swelling and pain of the right knee for 1 month", and finally diagnosed as synovial hemangioma; Case 9: Han * *, male, 13 years old, the chief complaint was "swelling and pain of joints for 1 month and fever for 1 week". Juvenile dermatomyositis was finally diagnosed; Case 10: Fang *, female, 11 years old, the chief complaint was "left sternoclavicular joint pain for 1 year and 2 months". MRI scan of the thoracic vertebrae showed changes in the 5th and 7th thoracic vertebrae, and pathological diagnosis (left clavicle mass and thoracic vertebrae) showed fibrous hyperplasia and Lymphocyte and histiocyte infiltration, so as to diagnose chronic recurrent multifocal osteomyelitis; Case 11: Ding * *, male, 8 years old, the chief complaint was "right knee pain for 2 months and fever for 1 month". The tests showed IgA < 0.0667g/l, IgG 3.51g/l, IgM 0.138g/l and lymphocyte absolute value 0.54 * 109 / L. The gene suggested PTPRC gene mutation and diagnosed severe combined immunodeficiency complicated with immunization related arthritis; Case 12: Li * *, male, 13 years old, the chief complaint was"rash and joint swelling for 4 years". The gene showed NOD2 mutation, and he was finally diagnosed Blau syndrome; Case 13: Meng * *, male, 7 years old, the chief complaint was "fever with swelling and pain of the right knee for 2 months". Articular fluid NGS indicates Acinetobacter Qiong and Staphylococcus aureus, and the final diagnosis was suppurative arthritis.
Conclusion: There are many diseases with joint symptoms, and clinicians need to distinguish them carefully to avoid falling into the trap of arthritis.

关键字 Juvenile Idiopathic Arthritis; joint;

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TRNT1 gene mutation leads to congenital sideroblastic anemia with immunodeficiency, fevers, and developmental delay (SIFD)

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Objective: To understand the characteristics of congenital sideroblastic anemia with immunedeficiency, fever, and developmental delay (SIFD) through the study of clinical manifestations and laboratory examinations.
Methods: Retrospective analyze the symptoms, signs and laboratory examinations of a child with SIFD caused by TRNT1 gene mutation treated in our hospital in June 2021, and concluded the clinical characteristics, diagnosis and treatment. Besides, the literature was reviewed.
Results: The child had periodic fever after birth with the highest body temperature of 39.5℃. The fever peak was 3-4 times a day for 5 days each time. The fever occurred again after 7 days when the body temperature was normal. Antibiotic treatment was ineffective. During fever, leukocytes increased, mainly neutrophils, and CRP increased significantly. When body temperature was normal, leukocytes and CRP decreased compared with that during fever, but they were still higher than normal. Fever was accompanied by diarrhea and vomiting, and the symptoms disappear when the body temperature returned to normal. During the course of the disease, there was a light red round rash on the face, and some of them were ulcerative and gradually spread to the whole body. The rash disappeared after being treated with gamma globulin and dexamethasone in the hospital. The patient had small cell hypochromic anemia and had thrombocytopenia once. In addition, he has growth retardation. The absolute value of T cells increases, while the absolute value of B cells decreases. The immunoglobulins, includes IgG, IgA and IgM, were decreased, and the Cytokines, like γ- IFN, IL-6 and IL-8, were increased. The whole exon gene sequencing (WES) showed that TRNT1, CHR3: 3189238, NM_182916; Exon7, c.907c > G (mother source); CHR3: 3170812, NM_181916; Exon2, c.88a > G (father source). According to the symptoms, signs and laboratory examination, the child was finally diagnosed as congenital sideroblastic anemia with immunodeficiency, fevers, and developmental delay. The child received gamma globulin and adalimumab. The body temperature returned to normal on the third day of fever, and the retested cytokines fell to the normal range.
Conclusion: TRNT1 is a nuclear gene encoding tRNA nucleotidyltransferase. tRNA nucleotidyltransferase is the basic prerequisite for mature tRNA aminoacylation and protein biosynthesis. The mutation of TRNT1 gene leads to abnormal metabolism of mitochondria and cytoplasm, which is characterized by SIFD syndrome. SIFD is an autosomal recessive disease with severe multiple organ involvement, which can be characterized by ferricytosis Anemia, B-cell immunodeficiency, periodic fever and growth retardation. Immunoglobulin replacement therapy is mainly used in patients with B-cell deficiency, which can reduce the risk of infection. TNF inhibitor (adalimumab) is also used in this case which effectively controlled the course of periodic fever and reduced the level of cytokines in peripheral blood, suggesting

that adalimumab is effective in the treatment of this disease. The pathogenesis of this disease needs to be further studied.

关键字 TRNT1，sideroblastic anemia，immunodeficiency, fevers, developmental delay

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Clinical characteristics and risk factors of recurrent Kawasaki disease

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Abstract Objective To summarize the clinical characteristics and explore the risk factors of recurrent Kawasaki disease. Methods In this retrospective study, we reviewed 41 cases with recurrent Kawasaki disease in Children′s Hospital of Chongqing Medical University from January 2013 to January 2021. And another 123 children with Kawasaki disease who had no recurrence during at least 6 years of follow-up were assigned into control group. Furthermore, the risk factors of recurrence were derived by comparing the clinical characteristics of recurrent cases at their initial episodes with those of control cases by Chi-square test and the Mann-Whitney U test, followed by Logistic regression and receiver operating characteristic analysis. Results There were 29 males and 12 females in 41 children with recurrent Kawasaki disease. Compared with the first episode,the second episode had lower white blood cell (15.2 (12.8 - 18.8)×109/L vs. 18.0 (14.9 - 23.4)×109/L, Z = -2.462, P = 0.014) and rate of edema in extremities (54% (22/41) vs. 76% (31/41), c2 = 4.321, P = 0.038), shorter fever durations before intravenous immunoglobulin treatment (5.0 (5.0 - 6.0)/d vs. 6.0 (5.0 - 7.5)/d, Z = -3.329, P = 0.001) and higher levels of hemoglobin ((116±8) vs. (107±12) g/L, t = -4.124,P ＜ 0.000) and albumin((39±5) g/L vs. (36±6) g/L, t = -3.009, P = 0.004). Multivariate logistic regression analysis showed that C-reaction protein ＞ 97.5 mg/L (OR = 3.014, 95% CI 1.350 - 6.730, P = 0.007), platelet ＞ 276 × 109/L (OR = 4.099, 95% CI 1.309 - 12.838, P = 0.015), intravenous immunoglobulin resistance (OR = 9.239， 95% CI 1.178 - 72.477, P = 0.034), Mycoplasma pneumoniae infection (OR = 2.585, 95% CI 1.129 - 5.922, P = 0.025) were independent risk factors for recurrent Kawasaki disease recurrence.The predictive model then was generated using these four risk factors. The receiver operating characteristic analysis found the area under curve was 0.732 (95% CI 0.647 - 0.817). When the cut-off was 0.241, the sensitivity and specificity were 63.4% and 70.7%, respectively. Conclusions Children with Kawasaki disease should be followed up for at least 2 years after the first episode and we should pay more attention to C-reaction protein. Children with Mycoplasma pneumoniae infection, intravenous immunoglobulin resistance, higher C-reaction protein and platelet at the first onset have a higher risk of recurrent Kawasaki disease.

关键字 粘膜皮肤淋巴结综合征；复发；危险因素；儿童

分类：13. Immunology 免疫
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Precision medicine for inborn error of Immunity

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Inborn errors of immunity (IEIs) are a group heterogeneous disorders caused by the inborn defects in one or more components of the immune system. Based on the nature of intrinsic defect, IEIs manifest as infections, as well as features of immune dysregulation such as autoimmunity, lymphoproliferation, autoinflammation and malignancy. According to the population prevalence, it is estimated there are around one million IEI patients in China. However, over 95% of them are unidentified. Even for those diagnosed, a large proportion of them have poor clinical outcome as a result of delayed diagnosis and inappropriate management. Therefore, the diagnosis and treatment are the two main hurdles for IEI management in China. In order to solve these problems, the author has been focusing on the translational research for the precision genetic diagnosis and targeted therapy of IEIs.

Previously, all the IEI-causative genes were reported by foreign research scholars. With the efforts, the author identified, for the first time in the world, a novel disease-causative gene, RasGRP1, in autoimmune lymphoproliferative syndrome-like disorder, which is also the first report of novel IEI gene in China. In addition, I reported novel mutation of IL10R1 in neonatal-onset Crohn's disease for the first time in Asia Pacific. Following our report, many other patients with IL10R mutation have been described in Asia Pacific. The author also identified novel STAT1 mutation in Penicillium marneffei infection, and NLRC4 mutation in mild autoinflammatory disease. These novel IEI-causative genes have been chosen and deposited in the worldwide renowned OMIMI database. More importantly, one of my studies was selected as an "advance in clinical immunology" by American Academy of Allergy, Asthma and Immunology; and one was selected as a best study in the field of pediatric Immunology in China.

Besides the genetic diagnosis, the author also devotes to the precision treatment of IEIs. Ig replacement is the cornerstone of therapy for patients with antibody deficiency. In order to unify this treatment throughout China, the author organized the Chinese Society of Pediatric Immunology to write a guideline on the Ig therapy in IEI patients. After clarifying the underlying mechanisms of LRBA and CTLA4 deficiency, a type of IEI of immune dysregulation, I successfully used abatacept as targeted therapy of such patients for the first time in Asia Pacific region, demonstrating a promising treatment modality. In addition, the author identified the frequency of cTfh cells as a sensitive marker for tracking disease activity and the response to abatacept therapy. Hematopoietic stem cell transplantation (HSCT) is a cure treatment for many IEIs. The author optimized the HSCT protocol for chronic granulomatous disease, which significantly improve the successful rate and survival.

With a small step forward during the past years, the author is committed to the precision medicine of IEI, and shall continue to promote the advancement of pediatric immunology.

关键字 inborn error of Immunity, Precision medicine, Immunology

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Effective therapy of tocilizumab on systemic juvenile idiopathic arthritis associated refractory macrophage activation syndrome

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Background: Macrophage activation syndrome (MAS) is a life-threatening complication of systemic juvenile idiopathic arthritis (sJIA) that remains difficult to treat. Even with conventional therapies, few patients still experience incomplete resolution of disease. Tocilizumab (TCZ) has been approved as a salvage therapy on sJIA-associated refractory MAS (sJIA-rMAS) in limited case reports. Here we report our experiences with TCZ in the treatment of sJIA-rMAS.
Methods: We retrospectively reviewed the charts of 6 patients diagnosed with sJIA-rMAS, who were treated with TCZ at our hospital from Jan 2016 to Jan 2020. Demographic, clinical, and laboratory characteristics and outcomes were recorded. Refractory MAS was defined empirically as failure to experience an adequate response to conventional therapy, which was considered as persistent or worsening symptoms and laboratory markers one week after traditional treatment. The laboratory findings were assessed before and within 7 days of intravenous TCZ including peripheral blood white blood cell count (WBC), hemoglobin (HB), platelet (PLT), c-reactive protein (CRP), erythrocyte sedimentation rate (ESR), albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum ferritin (SF), and fibrinogen (FIB).
Results: The age of sJIA-MAS diagnosed was 4.5 years (rang 1.4-9.7 years). Conventional therapies before TCZ including at least one course of intravenous methylprednisolone pulse (15-30 mg/kg/day for 3 days) combined at least one course of IVIG pulse (2g/kg) and intravenous or oral CsA. These therapies were effective in improving some of the clinical features, including skin rashes (4/5), lymphadenectasis (3/5), shock (1/1) and convulsion (1/1). However, other symptoms of fever (6/6), lymphadenectasis (2/6), coronary artery ectasia (2/6), myalgia (1/6) were persistent in sJIA-rMAS patients with development of gastrointestinal symptoms (4/6), polyserositis (1/6) during the disease progression. They had abnormal total WBC (6/6) with 3 higher and 3 lower than normal, mild anemia (6/6), refractory thrombocytopenia (1/6), extremely high CRP and ESR (4/6), hypoalbuminemia (4/6), higher ALT (2/6) or AST (1/6), extremely high SF (5/6) and low FIB (2/6) after conventional therapies. After treatment with TCZ, their clinical manifestations were favorably improved in 7 days with 5 patients got afebrile in 24 hours. Improvement in peripheral blood WBC, HB, CRP, ESR, albumin, ALT and AST became obvious within a week except for SF, FIB and PLT. There were no infusion-related adverse effects of TCZ in our study. The median follow-up was 29.7 months (range 15–46 months). No side effect and fatality were recorded in this series.
Conclusions: TCZ may be safe and effective for the treatment of sJIA-rMAS after the failure of the conventional therapies.

关键字 Tocilizumab, Systemic juvenile idiopathic arthritis, Macrophage activation syndrome

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Mesenteric vasculitis in children with systemic lupus erythematosus

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Objective:To analyze the clinical characteritics,diagnosis and treatment based on two lupus mesenteric vasculitis (LMV) case.
Methods: We report 2 cases of LMV and the clinical characteristics, laboratory examinations, images and treatments of these two cases are described.
Conclusion: The first one is a 14-year old girl with intermittent abdominal pain and vomiting for 4 months. She had suffered a laparotomy considering of indigitation in local hospital. After admission to our hospital, laboratory examinations showed elevated ANA titer (1:1000),positive anti-dsDNA, anti-SSA, anti-SSB antibodies with normal blood cell count. After a few days,she presented with low fever as well as neutropenia and low C4. So the diagnosis of SLE was considered and intravenous methylprednisolone of 40mg/d combined with oral hydroxychloroquine was administered. But after one week of treatment, the symptoms and signs relapsed. The abdominal computed tomography (CT) with contrast demonstrated diffuse bowel wall thickening and edema with target sign, prominently jejunum, engorgement of mesenteric vessels with comb sign, and ascites. After one pulse of methylprednisolone(750 mg/day for 3 days) and cyclophosphamide,her symptoms vanished and abdominal CT scan showed great improvement. Now she remains in remission with 6mg/day of methylprednisolone, hydroxychloroquine and mycophenolate mofetil after 6 times of cyclophosphamide. The second one is a 17-year-old girl who was diagnosed with SLE at the age of 10 and with the treatment of methylprednisolone, hydroxychloroquine and 6 times of cyclophosphamide,her course was stable for a few years.But she got fever and rash after 6 months of taking medications irregularly,as well as recurrently slight abdominal pain and diarrhea without paying enough attention. She received methylprednisolone increased to 30mg/day and intravenous belimumab,and her symptoms of fever and rash improved,with methylprednisolone tapered slowly to 8mg/day for 2 months. Then,she was readmitted to our department because of nausea and vomiting ,severe abdominal pain and diarrhea, described as ten to twenty watery stools per day for 3 days. After admission to our hospital,she felt frequent, urgent and painful urination. Laboratory examinations showed elevated ANA titer (1:1000),positive anti-dsDNA（＞800IU/ml） and low C3 and C4. CT demonstrated that the duodenum and small intestine walls thickened, her bilateral ureteropelvic dilated, and her bladder wall thickened too. CT and ultrasound also indicated abdominal effusion, pelvic effusion and pleural effusion. The signs and symptoms releived after one pulse of methylprednisolone(500mg/day for 3 days) and cyclophosphamide.
Discussion: Lupus mesenteric vasculitis(LMV) is a rare but severe gastrointestinal complication of systemic lupus erythematosus. Computed tomography (CT) scan is considered of the golden standard investigation of LMV. When children present with gastrointestinal symptoms with the involvement of other organs, especially the urinary system,antibodies and abdominal CT scans should be performed. Induction therapy with pulse steroids and IV cyclophosphamide, followed by long-term lower-dose steroids is better for the prognosis of the disease.

关键字 systemic lupus erythematosus, mesenteric vasculitis, gastrointestinal complication

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Case Report: A Patient from China with STING-Associated Vasculopathy with Onset in Infancy

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STING associated vasculopathy with onset in infancy (SAVI), caused by gain-of-function mutations in TMEM173, is characterized by widespread chronic inflammation affecting primarily the skin and lungs. A 1-year-old boy was admitted to our hospital with facial rashes, cough, failure to thrive and repeated oral ulcers. The inflammation indicators of the boy were normal or slightly elevated, while the immunoglobulin indicators were significantly elevated. Chest CT demonstrated infectious lesions in both lungs and whole genome sequencing confirmed a heterozygote mutation in the TMEM173 gene (c.463G>A, p.V155M). In conclusion, we describe a SAVI patient from China, representing typical clinical features, and the whole gene sequencing revealed a heterozygote mutation in the TMEM173 gene.

关键字 STING associated vasculopathy, TMEM173, autoinflammatory diseases

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Myeloid-derived suppressor cells depend on IL-1β promote Th17 cell differentiation in autoimmune arthritis

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Objective To elucidate the pathogenesis of autoimmune arthritis and find new therapeutic targets, We would use collagen induced arthritis (CIA) to investigate the role and mechanism of Myeloid-derived suppressor cells(MDSCs)on Th17 cell differentiation. **Methods** SPF grade male DBA1/J mices were randomly divided into CIA group (n=10) and control group(n=10),and An autoimmune arthritis mouse model was prepared by CIA method.The frequency of MDSCs and Th17 cells were examined in each group by flow cytometry,The level of plasma IL-1β、IL-10 and IL-17A were detected by ELISA ;The relative expression of related to Th17 differentiation factor:STAT3 mRNA, retinoic acid associated orphine receptor (ROR) alpha mRNA and ROR gamma t mRNA by Real-time fluorescence quantitative PCR. The effect of MDSCs on the differentiation of Th17 cells in CIA mice was assessed by the co-culture method of MDSCs and mouse naive CD4+T cells in the condition of Th17 cell differentiation(IL-6+TGF-β),And in some studies,IL-1βmAb or IL-1ra was added when coculturing MDSCs with CD4+T cells to observe the effect of MDSCs on the differentiation of Th17 cells. **Results** Compared with control group,the frequency of MDSCs,the level of the cytokines IL-1β、 IL-17、IL-10,the mRNA relative expression of RORγt were increased significantly ($P < 0.01$);and the frequency of MDSCs positive correlation with the Th17 cells numbers in CIA mice.MDSCs displaying T cell suppressive proliferation and secretion of gamma interferon (IFN-γ) in CIA,but MDSCs promoted Th17 cells differentiation in vitro under Th17 cells differentiation conditions,followed by significantly increased of IL-17A、IL-1β,and upregulation of STAT3 and RORγt.When blocking IL-1β signal can reduce the role of MDSCs in differentiation of Th17 cells. **Conclusion** Our studies show that MDSCs have the capacity to promote inflammatory by driving Th17 cell differentiation dependent on IL-1β in autoimmune arthritis.Therefore, MDSCs may be a target for autoimmune arthritis.

关键字 Myeloid-derived suppressor cells;IL-1β;Th17 cells; Collagen induced arthritis; Rheumatoid arthritis.

分类：13. Immunology 免疫
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Leflunomide Inhibition of proliferation and apoptosis of human cytomegalovirus infection in human embryonic lung fibroblasts

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Objective To explore the mechanism of Leflunomide(LEF) protecting human embryonic lung fibroblast injury,to provide the theory in LEF antiviral function to human cytomegalovirus (HCMV).**Methods** Control group, HCMV group,GCV+HCMV group,and LEF+HCMV group. Control group, containing 0.02% DMSO in RPMI 1640 culture medium,HCMV stimulation in cell culture medium by adding HCMV, GCV+HCMV treated group both in cell culture medium added GCV and HCMV, LEF+HCMV treated group both in cell culture medium added LEF and HCMV, after 24h, 48h and 72h and cell morphology was observed perturbation.Test proliferation and apoptosis of human cytomegalovirus infection in human embryonic lung fibroblasts by using MTT and flow cytometry. **Results** Add HCMV, cell proliferation happen significant inhibitory effect, compared with controls has obvious statistical significance ($P < 0.05$). Add GCV, along with the increase of concentration, cell proliferation inhibition effect significantly reduce, apoptosis rate to decrease, and HCMV group compared with obvious statistical significance ($P < 0.01$). Add LEF, cell proliferation inhibition effect reduced, and HCMV group compared with the statistical significance ($P < 0.05$). Different doses of LEF to human embryonic lung fibroblast proliferation has dose-response inhibition effect, the more obvious differences between groups of statistics ($P < 0.05$). In addition, HCMV infected human embryonic lung fibroblast apoptosis rate significantly increased, and with the passage of time, apoptosis rate increase obviously. Compared with controls with significant statistically significant ($P < 0.01$).Add LEF, apoptosis rate decreased, and compared with HCMV infection group statistical significance ($P < 0.05$).**Conclusion** Leflunomide protected the injury of human embryonic lung fibroblast with human cytomegalovirus infection,and significant inhibitted proliferation and apoptosis by HCMV infection, which to clarify the mechanism of LEF antiviral infection, and to provide experimental evidence to a new way to treat the immune disfunction patients with HCMV infection.

关键字 Leflunomide; human cytomegalovirus ;human embryonic lung fibroblast; apoptosis

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Study on the association between C159-T polymorphism in promoter region of CD14 and juvenile idiopathic arthritis

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Objective To investigates the distribution of CD14 promoter gene-C-159T polymorphism in Guangdong Han population of China and analyzes the association of CD14 polymorphisms with juvenile idiopathic arthritis (JIA).**Methods** genotypes of CD14 were determined in 104 JIA patients and 281 controls by Polymerase chain reaction-restriction fragment length polymorphism.**Results** CD14 promoter-159 genotype frequencies of CC,CT and TT in systemic JIA group were 10.87%,.41.30%,47.83%;and 12.50%,5.00%,37.50% in polyarticular JIA group;and 10.00%.,65.00%,25.00% in oligoarticular JIA and 7.14%,71.43%,21.43% in other JIA ;and in normal control group were 37.01%,46.98%,16.01%.Genotype distribution wan in accordance with Hardy-Weinberg equilibrium.There existed statistically significant dierence in frequencies of genotype and allele in CD14 C-159T polymorphism between systemic JIA group and conteol group,polyarticular JIA group and control group .There also existed statistically difference in frequencied of allele between oligoarticulad JIA group and control group.The T allele frequency of male and female were significantly higher than those in the control group(P<0.001 of both). **Conclusions** There existed statistically significant correlation of CD14 gene promoter region-159 polymorphism with systemic JIA and polyarticular JIA among Han population in Guangdong; the allele of the C-159T polymorphism of CD14 gene may be a risk factor for juvenile idiopathic arthritis in Han population.

关键字 CD14 promoter; single nucleotide polymorphism; juvenile idiopathic arthritis

Pediatric Intensive

& Critical Care

儿童危重症

分类：21. Pediatric Intensive & Critical Care 儿童危重症
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A protocol to develop a standard guideline for neonatal pain management

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Background: Hospitalized newborns experience a high frequency of painful procedures. Undertreated pain has a series of adverse physical and psychosocial effects on newborns. Guidelines successfully applied in clinical practice can effectively improve pain management in NICUs and reduce the incidence of pain. Neonatal care providers in China are in urgent need of a high-quality, evidence-based guideline for the treatment and management of neonatal pain. The National Clinical Research Center for Child Health and Disorders is leading the development of a standard guideline for neonatal pain management suitable for the medical environment in China providing empirical support and safety guarantees for clinical practice. The WHO Collaborating Centre for Guideline Implementation and Knowledge Translation will provide technical support and guidance. The purpose of this paper is to outline the detailed methodology and technical route of guideline development.
Methods: We will follow the WHO principles and methods for the formulation of standard guidelines. The critical steps for developing the guideline are as follows:(I) definition of the guideline Scope; (I)establishment of guideline working groups;(III) selection of the clinical questions; (IV) performance of systematic reviews; (V) grading the quality of the body of evidence; and (VI) formulating recommendations and reaching consensus.
Discussion: This protocol would ensure that the process of guideline development is normative, scientific, and transparent. The standard guideline for neonatal pain management based on the available high-quality evidence and tailored to the Chinese health care system will help neonatal caregivers in NICUs effectively manage neonatal pain.
Guideline registration: The guideline was registered at the International Practice Guidelines Registry Platform. The registration No.is IPGRP-2021CN044.

关键字 Practice guideline; Grading of Recommendations Assessment, Development, and Evaluation(GRADE); pain; newborn

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Different Dosages of Methylprednisolone Therapy for Acute Necrotizing Encephalopathy of Childhood: 6-year Multicenter Retrospective Study

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Background; Highly effective treatments for acute necrotizing encephalopathy of childhood (ANEC) remain elusive. Although the efficacy of steroids has been proven, the optimum dosage has not been identified. This work aimed to investigate the prognosis of ANEC associated with different dosages of methylprednisolone.
Methods: A multicenter retrospective study was conducted in four pediatric intensive care units from December 2014 to December 2020. All patients diagnosed with acute necrotizing encephalopathy aged from 29 days to 18 years old were included. Patients who did not receive methylprednisolone during hospitalization were excluded. On the basis of the initial dose of methylprednisolone, the participants were classified into low-dose (＜20 mg/kg/d) and high-dose (≥20 mg/kg/d) groups.
Results: Thirty-six patients were included, comprising 11 in the high-dose group and 25 in the low-dose group. The mortality of ANEC at discharge was 36.1% (13/36), and it was significantly lower in the high-dose group than the low-dose group (9.1% vs. 48.0%, P=0.031). High-dose methylprednisolone may reduce the risk of mortality rate at discharge in ANEC (OR=9.231, 95%CI: 1.023－83.331, P=0.048). The median duration of the initial dose of methylprednisolone was 3 days in both groups. The follow-up duration was 2 to 60 months. Full recovery was noted in 2 patients (18.2%, 2/11) in the high-dose group and 1 patient (4.0%, 1/25) in the low-dose group.
Conclusion: High-dose methylprednisolone pulse therapy (initial dose ≥ 20 mg/kg/d) may improve the prognosis of ANEC.

关键字 acute necrotizing encephalopathy, children, methylprednisolone, prognosis, multicenter study

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Clinical and molecular feature of S. aureus invasive infection amongst Chinese children: pvl associated with elevated inflammatory indicator

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Objective: This study aimed to perform a molecular characterization of S. aureus from invasive infection in China and assess the association of Panton-Valentine leukocidin (PVL) with clinical and molecular parameters.
Methods: S. aureus isolates causing invasive infections were obtained from Beijing Children's Hospital between January 2016 and December 2019. The isolates were typed using multi-locus sequence typing and staphylococcal protein A typing. For methicillin-resistant S. aureus isolates, staphylococcal cassette chromosome mec typing was conducted. Furthermore, all isolates were tested for antibiotic susceptibility by using agar dilution and E-test methods and the presence of pvl was detected via polymerase chain reaction. Corresponding clinical data were gathered using electronic medical records.
Results: A total of 152 invasive isolates were identified, in which 25 STs were determined and ST59 was the most prevalent genotype. Pvl genes were detected in 48.0% (73/152) of clinical isolates; amongst them, 46.6% (34/73) were community-acquired S. aureus. The resistance rate of cefuroxime and the multidrug resistance rate in pvl- isolates were much higher than those in pvl+ isolates (P = 0.02 and 0.04, respectively). The prevalence of patients who received antibiotic administration before admission was higher in pvl+ isolates than in pvl- isolates (P = 0.02). The pvl+ isolates demonstrated statistically higher white blood cell count, percent of neutrophil, C-reactive protein level and procalcitonin level than the pvl- isolates (P = 0.006, 0.04, 0.01 and 0.02, respectively).
Conclusion: This study investigated the association of pvl and the clinical index of S. aureus invasive infections. Results showed that pvl was associated with increased inflammatory indicators but it did not directly affect the clinical outcomes of patients. High prevalence of pvl was also found amongst S. aureus invasive isolates. ST22 had the highest pvl carriage rate amongst genotypes.

关键字 S. aureus, invasive infection, Panton-Valentine leukocidin, inflammatory indicator, pathogenicity.

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Acute respiratory distress syndrome and shock caused by severe chlorine gas poisoning was successfully cured by venous-arterial extracorporeal membrane oxygenation

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Objectives: To report a severe case of severe chlorine poisoning induced acute respiratory distress syndrome(ARDS) and shock requiring veno-arterial extracorporeal membrane oxygenation(V-A ECMO).
Design: Case report.
Setting: PICU in a china national children’s medical center.
Patients: A 11-year-old boy presenting with ARDS and shock was admitted to our PICU after inhaled chlorine poisoning.
Interventions: Veno-arterial extracorporeal membrane oxygenation.
Measurements and Main Results: After inhaling chlorine, the children quickly developed difficulty in inhalation, hypoxia, cyanosis and unconsciousness. After high-condition mechanical ventilation, hypoxia was only slightly improved for a short time, and then deteriorated rapidly and shock occurred. The highest oxygen saturation index was 27.3, and the chest X-ray showed extensive diffuse interstitial parenchyma changes in both lungs. With the support of VA-ECMO, the oxygenation and circulation of the children recovered quickly. The children received methylprednisolone 2mg/kg.d intravenous injection, the pulmonary lesions basically recovered 5 days after onset. He was successfully removed from the ventilator 1 day after the successful removal of ECMO. Follow-up 3 months after discharge showed the pulmonary lesions were completely absorbed, the physical activity returned to the basic level, and there were no other sequelae. ARDS is a severe complication of chlorine poisoning but has a good prognosis in most reports, only a few patients need venovenous ECMO support. Shock is a rare complication, which is considered to be caused by acute pulmonary heart disease in this case.
Conclusion: Chemical pneumonia caused by chlorine inhalation can lead to severe ARDS or even shock, but the prognosis is often good. ECMO support should be considered when conventional treatment is ineffective.

关键字 Chlorine poisoning, ECMO,ARDS, shock, children

分类：21. Pediatric Intensive & Critical Care 儿童危重症
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A retrospective study on the occurrence of early epilepsy in children with traumatic brain injury

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Objective: Early post-traumatic seizures (EPTS) refer to epileptic seizures occurring within one week after brain injury, which may induce secondary brain insults. This study aimed to define the risk factors for EPTS and the protective factors that could prevent its occurrence.
Design: A single-center retrospective study
Setting:Pediatric Intensive Care Unit, Beijing Children's Hospital,
Patients: Patients diagnosed with traumatic brain injury (TBI), admitted with and without EPTS in Pediatric Intensive Care Unit, Beijing Children’s Hospital between January 2016 and December 2020 were included in the study.
Interventions: None
Measurements and Main Results: We included 108 patients diagnosed with TBI. Among them, 35 patients were classified with EPTS and 73 with non-EPTS. Patients were categorized based on age, sex, mechanism of brain injury, cause of injury, presence of fever on admission, need for surgical intervention, and administration of hypertonic fluid therapy . We recorded the duration of mechanical ventilation, length of hospital stay, Glasgow coma scale score on admission and discharge, and cranial imaging findings. The overall EPTS incidence was 33.98% (35/108). In the EPTS group, there were 12 (34.29%) and 23 (65.71%) cases of open and closed craniocerebral injury, respectively (p = 0.022). Falls were the most common cause of TBI in both groups. The predominant imaging findings comprised brain contusion, diffuse axonal injury, intracranial hemorrhage, and multiple skull fractures. Logistic regression analysis revealed that closed craniocerebral injury and fever on admission were risk factors for EPTS, while surgical intervention and use of hypertonic saline were protective against its development. Patients aged four years or less had a higher incidence of EPTS.
Conclusions: Breakthrough EPTS occurred after severe TBI in 33.98 % of pediatric cases in our cohort. This is a higher seizure incidence than previously been reported. In our study we found patients with fever on admission and closed craniocerebral injuries have a higher incidence of EPTS. Hypertonic saline therapy and surgical intervention may be protective against the development of EPTS.

关键字 early post-traumatic seizures; traumatic brain injury; risk factors; children

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Clinical Application of Exome Sequencing for Monogenic Disorders in PICU of China

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Background. Exome sequencing (ES) has been widely used to detect genetic disorders in critically ill children. Relevant data are lacking in pediatric intensive care units (PICUs) of China. This study aimed to investigate the spectrum of monogenic disorders and the diagnostic yield and clinical utility of ES from a PICU in a large children's hospital of China.

Methods. From July 2017 to February 2020, ES was performed in 169 critically ill children with suspected monogenic diseases in the PICU of Beijing Children's Hospital. The clinical features, human phenotype ontology terms, and assessment of clinical impact were analyzed.

Results. The media age of the enrolled children was 10.5 months (range, 1 month to 14.8 years). After ES, a total of 43 patients (25.4%) were diagnosed with monogenic disorders. The most common categories of diseases were metabolic disease (32.6%), neuromuscular disease (18.6%), and multiple deformities (14.0%). The diagnosis yield of children with "metabolism/homeostasis disorder" and "growth delay" or "ocular anomalies" was higher than that of children without these features. In addition, the diagnosis rate increased when more features were observed in children. The results of ES had an impact on the treatment for 30 cases (69.8%): (1) change of treatment (n=11), (2) disease monitoring initiation (n=18), (3) other systemic evaluation (n=3), (4) family intervention (n=2), and (5) rehabilitation and redirection of care toward palliative care (n=12).

Conclusion. ES can be used as an effective diagnostic tool in the PICU of China and has an important impact on the treatment of patients with suspected monogenic conditions.

关键字 Exome sequencing; Pediatric intensive care unit; Monogenic disorders; Clinical application; Effective

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Circumferential subglottic hemangioma misdiagnosed twice in an infant with recurrent life-threatening dyspnea: case report

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OBJECTIVE: We reported a case of circumferential subglottic hemangioma (SGH) with recurrent life-threatening dyspnea in an infant, who was misdiagnosed as congenital laryngeal cartilage dysplasia firstly and then subglottic stenosis after tracheal intubation, to improve the understanding of atypical subglottic hemangioma.
METHODS: The medical history, examinations and treatments of a case of circumferential subglottic hemangioma presented to our hospital from January to March 2021 were analyzed, and the relevant literature was reviewed.
RESULTS: This case was a full-term, normal-born female infant with no abnormal birth history. Without any inducement, stridor occurred 21 days after birth, and she was admitted to another tertiary hospital at 25 days old due to progressive dyspnea. Diagnosed with pneumonia and suspicious laryngomalacia, she was given NCPAP and then intubation. However, she failed twice in removing intubation for reappearing dyspnea under NCPAP. Laryngoscopy revealed an inward aryepiglottic fold during inspiration and subglottic stenosis. Congenital laryngeal cartilage dysplasia was diagnosed. She was transferred to the PICU of our hospital at 1 month and 5 days old. After extubation on the 3rd day of admission, she was transferred to the Department of Respiratory, with continuous stridor but no dyspnea. Bronchoscopy revealed mucosal swelling, erosion, attachment of necrotic tissue in the subglottis, and hyperplasia of granulation tissue in the trachea, without signs of inward aryepiglottic fold. Acquired subglottic stenosis due to intubation was diagnosed while congenital laryngeal cartilage dysplasia was excluded. After treatments of steroids, stridor did't alleviate and the second bronchoscopy was performed, revealing a right-side predominant mucosal hypertrophy and membranoid hyperplasia, suggesting that subglottic stenosis did not relieve. Tracheal dilation with flexible bronchoscopy and tissue excision with cold knife were performed and the symptom of stridor was relieved. She was discharged under her parent's request 1 day later and did not have any follow-up visit. With barky cough, reappearance of dyspnea, and biphasic stridor, she was presented to the emergency room of our hospital at 3 months old. Laryngoscopy revealed a bulky lesion in right subglottis closing the glottis and subglottis. Due to progressive respiratory distress, we performed an anesthetic tracheal dilation and excision of the lesion with cold knife through flexible bronchoscopy, after which respiratory distress and stridor were alleviated. Specimens from the lesion were obtained for biopsy. However, while waiting for the pathology results, she developed intermittent strider and dyspnea again. On the 6th day of admission, the second anesthetic bronchoscopy was performed, which revealed a swelling vocal cord and sub-occlusive tissue hyperplasia in the right side of the subglottis. The tissue was incised with Nd;YAG laser, and stridor and dyspnea were alleviated. On the same day, transporter protein isoform 1 (GLUT1) was found to stain positively in the biopsy and SGH was therefore diagnosed. Enhanced CT imaging revealed a circumferential tissue thickening with contrast enhancement around the subglottic area, so the diagnosis of circumferential SGH was made. She was given propranolol 1mg/Kg/d orally, and the dose was gradually increased to 2mg/Kg/d. No

symptoms of strider or dyspnea reappeared and follow-up laryngoscopy showed continuous improvement of subglottic stenosis and a shrunken lesion.
Conclusion: Typical SGHs can be diagnosed by laryngoscopy or bronchoscopy, but atypical SGHs are easily misdiagnosed. Previous articles suggested that circumferential SGHs were risk factors for misdiagnosis. History of prolonged and repeated intubation also led to misdiagnosis. SGHs need to be considered in infants with croup-like symptoms and progressively stridor. When the diagnosis is in doubt, an enhanced CT scan and biopsy can help to clarify.

关键字 Circumferential subglottic hemangioma; Diagnosis error; Enhanced CT scan; Biopsy

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Evaluation of Extracorporeal Membrane Oxygenation in Children with Acute Hypoxemic Respiratory Failure in China: A Five-year Single-center Retrospective Study

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Objective: To summarize the clinical features, laboratory parameters, and outcomes of children with acute hypoxemic respiratory failure supported by extracorporeal membrane oxygenation (ECMO), and explore the risk factors for prognosis.
Methods: This retrospective study was conducted at the Pediatric Intensive Care Unit of the Children’s Hospital of Fudan University in China. Patients aged 28 days to 18 years with acute hypoxemic respiratory failure supported by mechanical ventilation who underwent ECMO between January 2015 and December 2019 were enrolled in this study. The primary outcome was in-hospital mortality within 28 days after admission. Demographics, medical history, comorbidities, laboratory findings, vital signs, medications, need for continuous renal replacement therapy, need for other rescue therapy, need for transportation, ventilator settings, and oxygenation indices were recorded. Appropriate data entry and statistical analyses were performed using access 2007 and SPSS software version 23.
Results: Fifty patients with severe acute hypoxemic respiratory failure were enrolled in the study. After excluding 5 patients with missing data, we analyzed 45 patients (90%). The overall mortality rate was 53%. The PaO2 prior to ECMO was higher (median [25–75% interquartile range]: 64 cmH2O [51.9–70.0 cmH2O] vs 55.1 cmH2O [43.8–60.1], p = 0.009) and oxygenation index prior to ECMO was lower (33.3 [30.1–40.7] vs 41.2 [33.2–55.1], p = 0.031) in survivor than in the non-survivor group. In the multivariate analysis, PaO2 prior to ECMO was significantly associated with survival (odds ratio: 1.129, 95% confidence interval: 1.022–1.247).
Conclusions: ECMO might be an alternative strategy for pediatric patients with severe acute hypoxemic respiratory failure. Low PaO2 prior to ECMO indicates a poor prognosis. Earlier implementation of ECMO should be considered in children with severe acute hypoxemic respiratory failure.

关键字 Acute hypoxemic respiratory failure, extracorporeal membrane oxygenation, pediatric intensive care unit, mortality

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Exosome Derived from Serum of Sepsis Children Induces Vascular Endothelial Cells Dysfunction Through the miRNA-30a-5p/DLL4/Notch1 Pathway

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Objectives
Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. The vascular endothelial cells dysfunction is one of the main pathophysiology during sepsis induced organ failure. In this study, we aimed to investigate the effect of exosomes derived from sepsis children on vascular endothelial and its related mechanism.
Methods
Exosomes, isolated from serum, were collected from sepsis children and healthy control children. After co-culturing with endothelial cells, vascular cell functions were detected by western blot. The internalization of exosomes, transfer of miR-30a-5p between endothelial cells was observed by immunofluorescence. Luciferase report assay, real-time qPCR, western blot, immunofluorescence, and immunohistochemistry staining were employed to explore the regulation of vascular cell function during sepsis by miR-30a-5p、DLL4 and Notch1.
Results
The results revealed that level of miR-30a-5p was increased in exosome derived from serum in sepsis children. In vitro, exosomes released from vascular endothelial cell stimulated with LPS can carry miR-30a-5p and transport to normal vascular endothelial cells. We confirmed that DLL4 was the target of miR-30a-5p. Furthermore, the effect of exosomal miR-30a-5p on endothelial cell was mediated by DLL4/Notch1. The inhibition of the activation of Notch1 signaling pathway in human vascular endothelial cells induced apoptosis, increase proliferation, decrease migration ability and downregulate permeability of human vascular endothelial cells.
Conclusions
Taken together, exosomes derived from the serum of sepsis children induced endothelial dysfunction through DLL4/Notch1signaling pathway. The results provide novel understanding of the function of exosomes in sepsis.

关键字 sepsis，endothelial dysfunction ，DLL4/Notch1signaling pathway

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Diagnosis of adenovirus and aspergillus co-infection in pediatric patients via next-generation sequencing: a case series study

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Background: Human adenovirus infection is common in young children, as they lack humoral immunity, as well as in immunocompromised and immunosuppressed individuals. In most cases, adenovirus infections are self-limiting but can also be fatal both in patients who are immunocompetent and immunocompromised. Aspergillus fumigatus is responsible for the development of life-threatening infections in immunocompromised populations, and manifests as an opportunistic pathogen in patients who are critically ill. Cases of adenovirus and Aspergillus co-infection in clinical practice are rarely reported.
Method: In this case series study, we have described cases in six children with clinical symptoms of pulmonary infection; etiology of the infections was attributed to adenovirus and Aspergillus co-infection and confirmed via unbiased metagenomic next-generation sequencing (mNGS).
Case presentation: Six children with fever and cough were admitted to the pediatric intensive care unit in Children’s Hospital of Fudan University. Adenovirus and Aspergillus co-infections were detected in all six patients by conducting microbiological culture, adenovirus antigen test, and mNGS analysis. After being subjected to treatments using antifungal agents and antiviral drugs, two patients died of infection whereas no deaths were reported during follow-up of the other four patients.
Conclusion: We reviewed six pediatric cases of severe pneumonia caused by adenovirus and Aspergillus co-infection. Our study suggests that mNGS can be used as a supplementary method for diagnosis of adenovirus and Aspergillus co-infection.

关键字 adenovirus, Aspergillus fumigatus, next-generation sequencing

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The Effect of Continuous Blood Purification on Children with Septic Shock: A Prospective Observational Study

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Objective To evaluate the efficacy of continuous blood purification in children with septic shock, and to further explore its effectiveness in children with septic shock without acute kidney injury (AKI). Methods We prospectively collected and analyzed the medical records of the children included in the study, including demographic data, treatment, laboratory examinations and prognosis. And we compared the prognosis and related organ dysfunction indicators of the blood purification group and the control group. Also, the patients without AKI were also assigned to the blood purification group and the control group, of which the prognosis was compares. Results This study included 80 patients diagnosed as septic shock admitted to the Children's Hospital of Fudan University, Children’s Hospital of Shanghai, Shanghai Children’s Medical Center, and Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine from January 2019 to December 2020. Of all patients, 59 cases were in the blood purification group and 21 cases were in the control group. There was no significant difference in the 28-day survival rate between the blood purification group and the control group (50.8% vs 57.1%, P>0.05). The change of heart rate and lactic acid in the control group 7 days after treatment was higher than that in the blood purification group, the difference was statistically significant (P<0.05), but the other indexes including blood pressure, coagulation function, kidney function, respiratory rate, lactic acid and infection parameters had on statistically difference between the two groups(P>0.05). In the blood purification group, the mortality rate of children with AKI was higher (P<0.05). Among children with septic shock without AKI, the survival rate of the control group was 75%, and the survival rate of the blood purification group was 60.9%, and the difference was not statistically significant (P>0.05). Conclusion For children with septic shock, especially those without AKI, the single-mode treatment of CBP may not improve the prognosis and its application is still to be discussed.

关键字 Septic shock; Children; Continuous blood purification

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Predictive value of diaphragmatic ultrasonography for the weaning outcome in mechanically ventilated children aged 1 to 3 years

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Objective To assess the value of each indicator of diaphragmatic ultrasonography in predicting the outcomes of ventilator weaning in 1-3 years old children with mechanical ventilation.
Methods A total of 72 children, who were mechanically ventilated and ready for weaning, from the pediatric intensive care unit (PICU) were enrolled in the study. Diaphragmatic ultrasonography was performed to the children for measuring and recording the diaphragm excursion (DE), contraction velocity, thickness, and diaphragm thickening fraction (DTF) in addition to the weaning outcome. The receiver operator characteristic (ROC) curves were used to assess the value of each indicator in predicting weaning success.
Results The area under the ROC curves (AUC) and the optimal threshold of each indicator were as followed: DE was 0.722, 8.08mm; DTFR was 0.711, 26.14%; DTFL was 0.710, 20.71%; DTFMIN was 0.782, 14.84%; DTFMAX was 0.787, 26.14%; DteiMAX was 0.714, 1.24mm; and contraction velocity was 0.652, 10mm/s.
Conclusion Diaphragmatic ultrasonography is feasible in guiding ventilator weaning, and the DE, DTF, DteiMAX indicators guide the weaning more accurately. Among them, DTF may be able to avoid the influence of diaphragm growth and development, acting as the most reliable predictor of weaning in children.

关键字 diaphragmatic ultrasonography; weaning ; children; critical illness

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Establishment of A Predictive Model for Nosocomial Infection in Pediatric Intensive Care Unit: A Real-world Study in China

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OBJECTIVE To establish a predictive model for NI using existing routine patient data.
METHODS We conducted a prospective, cohort 103-participant population study using clinician-recorded data from PICU of Children's Hospital of Fudan University in China, between June 2016 and March 2017. 85 patients admitted into PICU without NI were abstracted. Propensity score (P-score) was computed to match baseline characteristics of patients. Stepwise multiple logistic regression was performed to evaluate the association between possible predictors and NI. The receiver-operating characteristics (ROC) curve was performed to evaluate the predictive model. Results based on NI defined by Chinese diagnostic criterion (NICN) and US diagnostic criterion (NIUS) were compared as sensitivity analysis. Four predictors were associated with NI, a predictive model and its specific probability.
RESULTS Of 103 participants, 85 meeting the criteria were enrolled in this study, with males accounted for 57 episodes (67.1%). Their median age and weight were 39.0(IQR, 16.5 to 70.0) months and 13(IQR, 9.3 to 20.0) kg, respectively. According to the Chinese diagnostic criterion, 27 (31.7%) with NI (group NI) and 58 (68.3%) without NI (group No-NI). PRISMⅢ, arterial catheter and CRP at 48 hours after admission and P-score were analysed as significant predictors to NI, explaining 47.5% (R2=0.475, P<.001) of the outcome variation. The predictive model based on predictors has an AUC of 91.4% (95% CI, 85.1-97.7), a sensitivity of 75.86% (95% CI, 70.84-97.65), a specificity of 88.89% (95% CI, 62.83-86.13), and a PPV of 63.16% (95% CI, 45.99-78.19). Applying US diagnostic criterion, the same predictors can explain more (49.6% (R2=0.496, P<.001)) and the model has an AUC of 92.8% (95% CI, 87.2-98.5), a sensitivity of 82.86% (95% CI, 66.35-93.44), a specificity of 82.00% (95% CI, 68.56-91.42), and a PPV of 76.32(95% CI, 59.76-88.56).
CONCLUSIONS PRISMIII, arterial catheter and CRP at 48 hours after admission of PICU, and P-score were analysed as significant predictors to NI. Based on the predictors above, we propose a relatively simple, practicable model with good accuracy to predict NI. The accuracy remains if we define NI using US diagnostic criterion.

关键字 Pediatric Intensive Care Unit，Nosocomial Infection

分类：21. Pediatric Intensive & Critical Care 儿童危重症
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Metagenomic next-generation sequencing of bloodstream microbial cell-free nucleic acid in children with suspected sepsis in pediatric intensive care unit

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Bloodstream infection is a life-threatening complication in critically ill patients. Multi-drug resistant bacteria or fungi may increase the risk of invasive infections in hospitalized children and are difficult to treat in intensive care units. The purpose of this study was to use metagenomic next-generation sequencing (mNGS) to understand the bloodstream microbiomes of children with suspected sepsis in a pediatric intensive care unit (PICU). mNGS were performed on microbial cell-free nucleic acid from 34 children admitted to PICU, and potentially pathogenic microbes were identified. The associations of serological inflammation indicators, lymphocyte subpopulations, and other clinical phenotypes were also examined. mNGS of blood samples from children in PICU revealed potential eukaryotic microbial pathogens. The abundance of Pneumocystis jirovecii was positively correlated with a decrease in total white blood cell count and immunodeficiency. Hospital-acquired pneumonia patients showed a significant increase in blood bacterial species richness compared with community-acquired pneumonia children. The Shannon diversity of bloodstream bacteria was positively correlated with procalcitonin, and bloodstream virus richness (chao 1) was negatively correlated with C reactive protein. Microbial genome sequences from potential pathogens were detected in the bloodstream of children with suspected sepsis in PICU, suggesting the presence of bloodstream infections in these children.

关键字 Bloodstream infection, metagenomic next-generation sequencing, pediatric intensive care unit, Pneumocystis jirovecii

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Causes and Characteristics of Pediatric Unintentional Injuries in Emergency Department and its Implications for Prevention: A Cross-Sectional Study in Shanghai

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Objective: We conducted a cross-sectional study to investigate the epidemiologic characteristics and causes of the unintentionally injured child presenting to the emergency department in Shanghai, which expected to serve as the basis for a piece of in-depth evidence for the public health prevention control measures.
Methods: A cross-sectional study was conducted among children and adolescents (aged <18 years) with an unintentional injury who presented to the emergency department. The medical records and rescue records of the emergency children were reviewed in detail and the admission records were reviewed through the electronic health records (EHR) to determine their outcome. Data were analyzed using multivariate logistic models.
Results: A total of 29597 unintentional injuries cases were identified between Jan 2017 and Dec 2018, with male versus female ratio of 1.75. Unintentionally fall was the most common reason for unintentional injuries among both gender, accounting for 72.2% cases of unintentional injury, with 71.8% and 72.9% for males and females, respectively. Following fall, the frequency of observed mechanism of injury was sports (9.3%), foreign body (6.4%), struck (4.9%), transport (4.1%), poison (1.2%), cut or pierce (0.9%) and high fall (0.4%). A distinctive pattern of mechanisms of unintentional injuries between gender was documented, with sports was significantly higher in males than females (10.2% vs. 7.8%). Compared with Grade 3 patients of CTAS (Canadian Emergency Department Triage and Acuity Scale), Grade 2 (OR=2.99, 95%CI = 1.93-4.63, P<0.001) and Grade 1 (OR = 74.85, 95%CI = 12.93-433.14, P<0.001) patients had statistically higher risk of admission. For different types of injuries, compared with fall, foreign body (OR = 0.37, 95%CI = 0.27-0.51, P<0.001) and poison (OR = 0.10, 95%CI =0.04-0.29, P<0.001) had lower risk of in-hospital admission; while transport (OR =1.31, 95%CI = 1.07-1.59, P=0.008) and high fall (OR = 2.58. 95%CI =1.48-4.49, P<0.001) had significantly higher risk of admission.
Conclusion: Fall was the most common cause of unintentional injuries of child and adolescent in Shanghai. Variation in causes of injury by age group and gender is essential when developing prevention measures.

关键字 Pediatrics; Unintentional injury; Causes; Emergency department; Cross-sectional study

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Importance of Early Genetic Sequencing in Critically Ill Neonates with Recurrent Hypernatremia: Results of a Prospective Cohort Study

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Objectives: The genetic characteristics in critically ill neonates with recurrent hypernatremia remained unknown. We aimed to implement early genetic sequencing to identify possible genetic etiologies, optimize the treatment and improve the outcome.
Methods: We prospectively performed exome sequencing or targeted panel sequencing on neonates diagnosed with recurrent hypernatremia (plasma sodium ≥150 mEq/L, ≥2 episodes) from January 1st, 2016 to June 30th, 2020.
Results: Among 22375 critically ill neonates, approximately 0.33% (73/22375) developed hypernatremia. The incidence of hypernatremia >14 days and ≤14 days was 0.03% and 0.3%, respectively. Among 38 neonates who had ≥2 hypernatremia episodes, parents of 28 patients consented for sequencing. Genetic diagnosis was achieved in 25% neonates (7/28). Precision medicine treatment was performed in 85.7% (6/7) of the patients, including hydrochlorothiazide and indomethacin for 57.1% (4/7) with AVPR2 deficiency; a special diet of fructose formula for one patient with SLC5A1 deficiency (1/7, 14.3%); and kallikrein inhibiting ointment for one patient with SPINK5 deficiency (1/7, 14.3%). Only hypernatremia onset age (adjusted odds ratio (aOR) 1.32 [1.01－1.72], p=0.040) independently predicted the underlying genetic etiology. The risk of a genetic etiology of hypernatremia was 9.0 times higher for neonates with a hypernatremia onset age ≥17.5 days (95% CI, 1.1-73.2; p=0.038).
Conclusions: Single-gene disorders are common in neonates with recurrent hypernatremia, and >50% of cases are caused by AVPR2 deficiency-associated congenital nephrogenic diabetes insipidus. Early genetic sequencing can improve therapy and outcome.
Trial registration number: NCT03931707, The China Neonatal Genomes Project (CNGP)

关键字 neonate; hypernatremia; genetics; congenital nephrogenic diabetes insipidus; congenital glucose galactose malabsorption

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Human breastmilk feeding in necrotising enterocolitis patients with surgical treatment A retrospective chart review study

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Background
One of the surgical treatments for necrotising enterocolitis (NEC) is to resect the necrotic bowel and defunction the gut by stoma, which can come with severe complications impacting infant growth. Human breastmilk feeding has been proved to prevent NEC, world-widely. This study is to identify whether human breastmilk could protect NEC patients against surgical stoma related complications.
Methods
A retrospective chart review was done on patients who had intestine resection and stoma for NEC in the period from 2015-1-1 to 2021-4-30 at Anhui Provincial Children’s Hospital (APCH). Demographics, feeding methods (human milk feeding versus formula milk feeding) and stoma related complications were collected, and the risk factors of stoma related complications were analysed.
Results
A total of 58 patients, including 35 males and 23 females, had stoma for NEC. The mean gestational age was 34 weeks (28 to 40). The mean body weight at surgery was 2.83kg (1.03 to 4.80). Before surgery, 38 patients had perforation. Additionally, 46 patients had ileostomy; 12 had colostomy. After primary operation, 40 of them were fed with human breastmilk while 18 of them were fed with formula milk. 26 of 58 patients had stoma related complications, including fluid/electronic imbalance, stoma prolapse, and stoma stenosis. Feeding methods and gestational age were found significantly related to stoma related complications via a binary logistical multivariable analysis.
Conclusions
In this study, the most frequent stoma related complication was fluid/electronic imbalance. Younger gestational age was identified as a risk factor for stoma related complications; human breastmilk feeding can protect patients against these complications.

关键字 human breastmilk feeding，necrotising enterocolitis，complication

分类：21. Pediatric Intensive & Critical Care 儿童危重症
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Clinical Features and Factors Associated wih Sepsis-Associated Encephalopathy in Children: Retrospective Single-Center Clinical Study

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Abstract:
Background: Septic-associated encephalopathy(SAE) is a common complication in septic patients with higher ICU and hospital mortality in adults,and also with poorer long-term outcomes.Clinical presentation may range from mild confusion to convulsions and deep coma.However,not much is known about SAE in children.We aimed to retrospectively analyze the data for children with sepsis,to illustrate the epidemiology,performance,adverse outcome and and evaluate the association between risk factors and SAE in children.
Results: A total of 217 patients with sepsis were retrospectively assigned to the SAE and non-SAE groups. 78 (43.6%) were diagnosed with SAE,and the mortality was 6.0% (13/78). There were significant differences in modified Glasgow Coma Scale (GCS) score, hemoglobin, platelets, total protein, serum calcium, international normalized ratio (INR), prothrombin time(PT), activated partial thromboplastin time (APTT), alanine amiotransferase (ALT) and procalcitonin (PCT) ($P<0.05$). The incidence of Septic Shock,Acute Kidney Disease,Liver Dysfunction and Coagulation were higher in SAE group. Both the GCS score, total protein and Liver Dysfunction were independent risk factors for SAE in pediatric with sepsis ($P<0.05$). The mechanical ventilation time [(7.11±17.95d)vs. (2.28d±5.82d), $P<0.001$], CRRT time [(2.20±7.30d)vs. (0.08±0.47d), $P<0.001$], ICU stay time [(304.38±480.40h)vs. (189.68±235.53h),$P=0.002$] had longer than the non-SAE.
Conclusions: The incidence of SAE in children is high and the prognosis is poor. Therefore, it is necessary to improve the awareness of SAE and reduce the risk factors to reduce the incidence of SAE.

Keywords: Sepsis, Sepsis-associated encephalopathy, Children, Risk factor

关键字 Sepsis, Sepsis-associated encephalopathy, Children, Risk factor

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Mortality Risk Factors in Children With Influenza-associated Encephalopathy Admitted to the Pediatric Intensive Care Unit Between 2009-2021

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Abstract
Background: Influenza-associated encephalopathy (IAE) progresses rapidly and has high mortality. The purpose of this study was to determine the risk factors for death in children with IAE in the pediatric intensive care unit (PICU).
Methods: Forty-six pediatric patients with IAE admitted to the PICU at Shenzhen Children's Hospital between December 2009 and January 2021 were evaluated. The information on clinical features, laboratory data, and prognoses of all patients was collected for further analysis. The next step was to transcribe and analyze the relevant data. The statistical study was performed using SPSS 22.0.
Results: A total of 46 patients were admitted to the Pediatric Intensive Care Unit (PICU), largely because of seizures or seizures accompanied by neurological signs (30.4%, 14/46) and sopor/coma (23.9%, 11/46). The children' median age was 4.0 years (interquartile range, 2.0－7.0 years). All included patients were diagnosed with influenza A virus. Of them, 29 patients (63%) survived, 17 patients (37%) died, and 32 patients (69.6%) developed neurological symptoms within 1－2 days of contracting fever. Common symptoms included fever (97.8%, 45/46), altered consciousness (84.8%, 39/46), seizures (67.4%, 31/46), cough (41.3%, 19/46), and vomiting (34.8%, 16/46). Old age, vomiting, >3 seizures/status epilepticus, sopor/coma, lymphopenia (lymphocyte count<0.8×109/L), increased alanine aminotransferase level (>100 IU/L), increased lactate dehydrogenase level (>500 IU/L), increased aspartate aminotransferase level (>100 IU/L), prolonged activated partial thromboplastin time (>40.7S), abnormal serum sodium level (<135 mg/L/>145 mg/L), and hematuresis/proteinuria were associated with poor outcome. A total of 45 cases underwent brain MRI/CT examinations. Radiologic imaging findings were abnormal in 11 (64.7%) non-survivors, mainly including symmetrical injuries of the thalamus, brainstem and cerebellum, cerebral cortex, and cerebral edema. Of 46 patients with IAE, 58.7% (27/46) stayed in the hospital for >7 days, and of the 17 children who died, 70.6% (12/17) died within one week of hospitalization. There were no statistically significant differences between survivors and non-survivors in the matter of time and dose of gamma globulin, megalosone (p> 0.05). Multivariate logistic regression analysis depicted that vomiting (OR = 11.71), >3 seizures/status epilepticus (OR = 11.93), and sopor/coma (OR = 24.49) is a prognostic variable and is mainly independently related to mortality.
Conclusions:Vomiting, >3seizures/status epilepticus, and sopor/coma were the predictive variables independently related to mortality.

关键字 Encephalopathy; Influenza; Neurologic manifestation; Children; Seizures; Death; Clinical characteristics

分类：21. Pediatric Intensive & Critical Care 儿童危重症
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A 4-Year-Old Boy With Down Syndrome Developed Plastic Bronchitis After Accidentally Ingesting Glue

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Background: Children under 3 years old usually swallow foreign bodies. Coins are the most common foreign bodies swallowed by children that seek medical attention in the United States, and fish bones are the most common in other countries. Preschoolers, adolescent boys, and children with mental health problems are at the highest risk.
Case Presentation: Herein, we described a 4-year-old Down syndrome boy was admitted to ICU for unexpectedly ingesting glue for 9 hours (04:33 on July 17, 2021). However, specific composition and ingested amount of the glue were unknown. After mistaking glue at about 19:30 on July 16, he had coughing, vomiting 3-4 times and dysphagia. After the child was admitted to the hospital, we opened the emergency rescue channel to complete the preoperative examination quickly. The otolaryngologist first performed a rigid bronchoscopy and removed part of the glue. However, subsequent chest CT showed that there were still foreign bodies in the deep lungs, so the microscopist performed a flexible bronchoscopy. The formation of “plastic bronchus” was surprisingly spotted. The “plastic bronchus” was smoothly taken out, and bronchuses were lavaged several times.
Conclusions: Exogenous plastic bronchus has never been reported, and the specific causes need to be studied further. For children who accidentally ingest chemical preparations, in addition to paying attention to burns to the esophagus, airway and gastric mucosa, if the obstruction of the airway persists, an in-depth examination of flexible bronchoscopy is necessary and can play a crucial role in diagnosis and treatment.

关键字 Foreign bodies, Plastic bronchus, Rigid bronchoscopy, Soft bronchoscopy, Down syndrome

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Analysis of the current situation of pediatric severe diseases in hospitals at all levels in our province during the COVID-19 epidemic period

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Objective: By analyzing the current situation of pediatric acute and severe diseases in medical institutions at all levels in our province under the epidemic situation, to provide reference for dealing with public health emergencies, discipline construction and medical quality management.
Methods: survey time: from January 1 to December 31, 2020; Respondents: 34 medical institutions with pediatric emergency / PICU / NICU in Jiangxi Province; Data source: Quality control monitoring data were selected from children's intensive care medicine major (emergency department, PICU and NICU) in 19 secondary and above hospitals in our province in 2020, Including 3 provincial hospitals, 11 municipal hospitals and 5 county hospitals (including 5 maternal and child health hospitals).
Results: 1. Statistical data showed that there were more emergency children in provincial Children's Hospital(1025601 cases), followed by provincial general hospitals (65237cases) and municipal Children's Hospitals (39928 cases). Specialized hospitals were more emergency children than general hospitals at the same level. No matter horizontal or vertical comparison, provincial hospitals have more patients of grade 2-3 (more than 59-69%), and most county and municipal hospitals have non emergency patients of grade IV (45-99.8%). 2. The death causes of emergency children in provincial and municipal hospitals are mainly respiratory cardiac arrest, followed by various accidental injuries (including tracheal foreign bodies, drowning syndrome, high-altitude falling injury, etc.) and premature infants. 3. The death causes of NICU children in hospitals at all levels were mainly acute respiratory failure, followed by acute heart failure, pulmonary hemorrhage, severe hypoxic-ischemic encephalopathy, etc. the primary diseases of NICU children in hospitals at all levels were mainly premature infant related diseases and severe neonatal asphyxia, followed by neonatal respiratory distress syndrome, neonatal meconium aspiration syndrome, neonatal pneumonia, complex heart disease, Severe genetic metabolic diseases, etc. 4. Children with septic shock tend to increase in NICU and PICU in hospitals at all levels. There were more critical and difficult patients in NICU and PICU in provincial hospitals. Therefore, its bed utilization rate (113%), average hospitalization day (16.69 days) is higher than city (12.75 days), county hospitals (80%, 7 days). In addition multiple antibiotic resistance bacteria infection (24 cases), total number of multidisciplinary clinical ward rounds (92 cases), and the return rate within 48 hours after transfer out of NICU (0.78%) were also higher than those in county-level hospitals (1, 2, 0).
Conclusion: 1. The proportion of grade IV non-acute patients in emergency and ICU of many hospitals is still high, Further optimization needs to be achieved in terms of operational and medical costs. 2. strengthening environmental hygiene in schools and kindergartens, reducing crowd concentration and wearing masks and hand washing can effectively reduce the incidence rate of pediatric infectious diseases. 3. The prevention and control of nosocomial infection should be strengthened to reduce the number of nosocomial infection cases in NICU. 4. Medical institutions at all levels should strengthen the training and research of sepsis, acute respiratory failure,

acute heart failure, pulmonary hemorrhage and severe hypoxic-ischemic encephalopathy, so as to achieve early detection, early diagnosis and timely treatment.

关键字 Epidemic situation, pediatric severe, medical quality

分类：21. Pediatric Intensive & Critical Care 儿童危重症
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Risk factors analysis of pediatric severe pneumonia complicated with sepsis in PICU

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Objective: To explore the risk factors of pediatric severe pneumonia complicated with sepsis in PICU.
Method: The clinical data of community-acquired severe pneumonia in the children's intensive care unit (PICU) of Jiangxi Children's Hospital from January 10,2014 to November 1, 2019 were analyzed retrospectively in Jiangxi Children's Hospital.
Result: The average age of 174 children was 16 ± 26.62 months, and 71.8% of them were severe pneumonia; The hospital stay in sepsis group (14.36 ± 15.03 days) was lower than that in non sepsis group (18.8 ± 17.72 days, $P < 0.02$). The mortality in sepsis group (43.7%) was higher than that in non sepsis group (15.0%, $P = 0.001$); The PCIs score of sepsis group was lower than that of non sepsis group ($P = 0.001$), of which 116 cases (66.8%) were complicated with basic diseases, including congenital heart disease (83.9% vs.46.0%, $P = 0.001$) and blood tumor disease in sepsis group (11.5% vs.1.1%, $P = 0.005$) were significantly higher than those in non sepsis group.174 blood cultures were positive in 39 cases (22.4%), mainly Staphylococcus (56.4%) and Streptococcus pneumoniae (17.9%). The bacterial infection in sepsis group was higher than that in non sepsis group (78.7% vs 21.3%, $P < 0.001$). 90 cases (51.7%) were positive for respiratory syncytial virus and cytomegalovirus, accounting for 42.2% and 40.0% respectively; There were 41 cases of mixed pathogen infection (23.7%), most of which were bacterial and viral mixed infection (15.6%), and the mixed infection in sepsis group (65.9%) was higher than that in non sepsis group (34.1%, $P = 0.02$).Univariate risk factor analysis showed that PCIs score, congenital heart disease, blood tumor disease, bacterial infection, virus infection, mixed infection, WBC, Hb, PLT, ALB, TBIL, bun, AST, K +, PCT, PaO_2, Cr and CRP were suspected risk factors for sepsis of severe pneumonia ($P < 0.05$). Multivariate analysis showed that congenital heart disease, bacterial infection, mixed infection, elevated WBC, elevated ast, decreased PO_2 and decreased PLT were independent risk factors of severe pneumonia complicated with sepsis.
Conclusion: Infants are at high risk of severe pneumonia. When severe pneumonia complicated with sepsis, the disease progresses rapidly, the length of hospital stay is short, the mortality is high and the prognosis is poor. Children with severe pneumonia complicated with sepsis are prone to organ failure, mainly acute respiratory failure and heart failure. Whether complicated with sepsis can be used as an indicator of poor prognosis of severe pneumonia. Congenital heart disease, bacterial infection, mixed infection, elevated WBC, elevated ast, decreased PO_2 and decreased PLT were independent risk factors
for severe pneumonia complicated with toxemia.

关键字 Severe pneumonia in children, Sepsis, Risk factors

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Predictive value of inferior vena cava variability on fluid responsiveness in children with septic shock undergoing mechanical ventilation

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This prospective study aimed to investigate the predictive utility of inferior vena cava variability on fluid responsiveness in children with septic shock undergoing mechanical ventilation. We enrolled 72 patients from the tertiary pediatric intensive care unit of a university-affiliated hospital in Chengdu, China. The patients underwent volume expansion (VE) after the diagnosis of septic shock. Further, 10–20 ml/kg of saline was infused intravenously within 30 minutes. Among the 72 enrolled patients, 30 responded to VE, while the remaining did not. Fluid responsiveness was defined as a ≥ 15% increase in the variation of velocity-time integral (ΔVTI). Central venous pressure (CVP) was measured through catheterization of the right internal jugular vein. Hemodynamics indexes, including ΔVTI, variability (ΔIVC), and inferior vena cava expansion index (dIVC), were determined through bedside ultrasound examination. Patients with fluid responsiveness showed significantly decreased ΔIVC and dIVC after VE ($P < 0.01$). All patients showed significantly increased CVP after VE ($P < 0.01$). The area under the curve of ΔCVP (CVPVEafter - CVPVEbefore) for predicting fluid responsiveness was 0.324. A cut-off value of ΔIVC > 21.83% for detecting fluid responsiveness yielded a sensitivity and specificity of 94.4% and 73%, respectively, with the corresponding values for dIVC being 88.9% and 60%. Our findings demonstrated that ΔIVC can reliably predict fluid responsiveness, with better sensitivity and specificity than dIVC.

关键字 Shock; septic; volume responsiveness; inferior vena caval; mechanical ventilation; bedside ultrasound

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三种危重症评分在脓毒症性急性肾损伤病情评估中的比较研究

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Introduction: Sepsis is the most common critical illness in clinical settings, and septic acute kidney injury (AKI) is a major cause of mortality in pediatric patient.
Methods: We aimed to investigate scoring systems for determining the severity of septic AKI through mortality prediction using Pediatric Risk of Mortality III (PRISM III), Pediatric Multiple Organ Dysfunction Score (P-MODS), and Pediatric Critical Illness Score (PCIS). The clinical data of 102 pediatric patients with septic AKI admitted to the pediatric intensive care unit from January 2014 to December 2018 were collected. Receiver operating characteristic (ROC) curves were plotted to determine the optimal cutoff values of the scoring systems for assessing mortality.
Results: There were 25.64% death rates among patients with stage 1 disease, 45% with stage 2 disease, and 58.14% with stage 3 disease, with a significant difference ($x2=8.8409$, $p=0.012$). The cutoff values of the ROC curves of PRISM III, P-MODS, and PCIS were 12, 6, and 82, respectively, in patients with unstaged septic AKI; 12, 5, and 84, respectively, in patients with stage 1 septic AKI; 17, 9, and 72, respectively, in patients with stage 2 septic AKI; and 12, 7, and 74, respectively, in patients with stage 3 septic AKI.
Conclusions: PRISM III was the best mortality risk assessment system for pediatric patients with unstaged septic AKI. PCIS was better in predicting the mortality risk of pediatric patients with stage 1 AKI, whereas PRISM III was better for pediatric patients with stage 2 and 3 AKI.

关键字 Sepsis; Acute kidney injury; Pediatric Risk of Mortality III; Pediatric Multiple Organ Dysfunction Score; Pediatric Critical Illness Score

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Establishment of a nomogram model for predicting the death risk of postoperative in children with complex congenital heart disease

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Background： Complex congenital heart disease (CCHD) is one of the major death causes of neonatal and infant , and surgery is the main method for the treatment of them. However, the postoperative condition of children changes rapidly, and the risk of cardiac arrest increases significantly. Therefore, early screening of CCHD cases that may lead to death is of great significance to reduce the postoperative mortality and disability rate.

Objective: The aim of this study was to establish a nomogram model for predicting the death risk of postoperative in children with complex congenital heart disease.

Methods: The clinical data of patients who underwent cardiopulmonary bypass thoracotomy surgery for CCHD in our hospital from January 2018 to December 2019 were retrospectively analyzed, independent risk factors for postoperative death of CCHD children were screened, and a nomogram prediction model was established based on the screening results. Then the prediction accuracy of the model was verified.

Results: Logistic regression analysis showed that IS (OR=1.113,95%CI:1.055~1.175)、WBC(OR=1.140,95%CI:1.044~1.245)、HB(OR= 0.973,95%CI: 0.949~0.998)、ALB(OR=0.907,95%CI:0.838~0.983) and CPR-Preoperative(OR= 36.656, 95%CI: 5.187 ~259.037) were independent death risk factors for CCHD children after surgery. A nomogram model was established based on the above independent risk factors. The model verification showed that the C-index was 0.898, the AUC was 0.899(95%CI:0.821~0.976), and the calibration curve was close to the ideal curve, indicating that the nomogram model had a good predicted accuracy. Whatmore, the model optimal cut-off was 36.

Conclusion: IS、WBC、HB、ALB and CPR-pre were independent death risk factors affecting CCHD children after surgery. The nomogram model constructed based on the risk factors in this article has a good predictive accuracy, and the patients with rating scores≥36 should be paid much more attention to, which can provide more aggressive treatment to improve the prognosis of children.

关键字 Complex congenital heart disease;Postoperative death;Risk model;Nomogram

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Analysis of the relationship between preoperative arterial oxygen partial pressure and acute kidney injury after surgery for tetralogy of Fallot and explore the related risk factors

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Background: Acute kidney injury (AKI) is a severe complication of pediatric cardiothoracic surgery. It is debatable whether patients with the low preoperative arterial partial pressure of oxygen (PaO2) are more likely to develop AKI. The study aims to investigate the incidence and possible influencing factors of AKI in patients who underwent the radical operation of tetralogy of Fallot (TOF) with different preoperative PaO2.
Methods: In this retrospective clinical study, 36 pediatric patients who underwent cardiothoracic surgery were enrolled in this study. The patients were divided into four groups according to preoperative PaO2. We examined the baseline data and outcomes of the study population among groups.
Results: Of the 36 patients, 17 developed AKI. Compared with the high preoperative PaO2 group, the low preoperative PaO2 group trended toward more severe and persistent acute kidney injury, but there was no significant difference in acute kidney injury among groups ($P>0.05$). In the 48-hour continuous monitoring after surgery, the oxygen metabolism indexes (Pv-aCO2/Ca-vO2) were correlated with AKI and there were significant differences among the groups.
Conclusions:
There is limited data from 36 patients to determine the effect of preoperative PaO2 on postoperative AKI. We did not find a statistically significant association between preoperative serum PaO2 levels and the incidence of postoperative AKI. Pv-aCO2/Ca-vO2 measured after cardiothoracic surgery was associated with subsequent acute kidney injury.

关键字 hypoxic tolerance, acute kidney injury, cardiothoracic surgery, postoperative, pediatric

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Association between prolonged vancomycin infusion period and the trough concentrations and nephrotoxicity in children

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Objectives: Vancomycin is an important choice for severe pediatric infections and nephrotoxicity remains an issue. The present study explored the optimal dosage and nephrotoxicity of vancomycin with different infusion periods in children.
Methods: This retrospective cohort study included pediatric patients who received vancomycin between June 2017 and June 2020 at Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine. Demographic details, infusion period, serum creatinine, duration of vancomycin therapy, trough concentration of vancomycin, area under the curve (AUC) of vancomycin, and intensive care unit (ICU) stay were reviewed.
Results: Sixty-eight children were included: 31 and 37 in the SII and PI groups, respectively. The trough concentration, the AUC values, and the target attainment were higher with PI compared with SII (P=0.02, P=0.01, and P=0.001, respectively). There were no significant differences between the SII and PI groups regarding the final creatinine, the peak creatinine, and the time to reach the peak creatinine (all P>0.05). None of the patients developed AKI. There were no differences between the SII and PI groups regarding the failure events, PICU stay, and duration of vancomycin therapy. The multivariable analysis showed that PI was significantly associated with trough serum concentrations of vancomycin (OR=2.26, 95%CI: 1.26-4.03, P=0.006).
Conclusion: Compared with SII, the PI strategy could increase trough concentration, AUC value, and target attainment in children treated with vancomycin. No obvious nephrotoxicity was observed.

关键字 vancomycin; infusion period; trough concentration; area under the curve; nephrotoxicity.

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Genome Sequencing Reveals A Delay Diagnosis of X-linked Hyper-IgM Syndrome presenting as Community-Acquired Pseudomonas aeruginosa pneumonia-related septic shock: A case report and literature review

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Pseudomonas aeruginosa, (P. aeruginosa) is a gram-negative aerobic bacterium, which is one of the major pathogenic bacteria in hospital-acquired infection. It is rarely seen in community-acquired infection, but attention should be paid to its high mortality and invasive progress.X-linked hyper-IgM syndrome (XHIGM; HIGM1; OMIM:308230) is one type of primary immunodeficiency diseases(PIDs).We report a patient who developed a particularly severe community-acquired P. aeruginosa pneumonia-related septic shock and a delay diagnosis of X-linked hyper IgM syndrome was made by genome sequencing.Fatal community-acquired P. aeruginosa infections in children, including previously healthy children, should be considered to search for underlying PIDs by exome/genome sequencing.

关键字 Pseudomonas aeruginosa,XHIGM,PID,exome/genome sequencing

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A case-control study on the relationship between humoral immune response and prognosis in children with severe sepsis

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【Abstract】 Objective To investigate the correlation between lymphocyte count, cytokine concentration and the severity、prognosis of severe sepsis children. Methods This was a retrospective study including 36 severe sepsis children admitted to pediatric intensive care unit between 2018.01.01 and 2019.12. 31. Firstly, the children enrolled in our study was divided into two groups depending the outcomes (death or survival). The differences of lymphocyte count, cytokine concentration between groups were analyzed. Results (1) Of the 36 children included in the analysis, 28 survived and 8 died. The death group had a shorter hospital stay than the survival group. (2) Compared with the survival children, the proportion of CD4+ lymphocytes in death children decreased on the first day of ICU admission ($p<0.05$), the concentrations of IL-1β、IL-2、IL-6、IL-8 and IL-10 were increased ($p<0.05$). There was no significant difference in absolute count of CD3+, CD4+, CD8+ and other lymphocyte subtypes between the two groups. (3) The results of logistic regression analysis suggested that increased IL-10 level would increase the risk of death in children.
Conclusions In children with severe sepsis, both proinflammatory factors and anti-inflammatory factors were expressed in the early stage of the disease, and mixed inflammatory response syndrome appeared in the children. However, the high expression of IL-10 and the decreased proportion of CD4+T lymphocytes suggest that the immune function of children is inhibited, which will increase the risk of death of children.

关键字 Sepsis; Lymphocyte; Cytokine; Immune dysfunction

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The Profile of COMFORT score, SBS, FLACC scale, and NVPS among Mechanically Ventilated Pediatric Patients in PICU in Indonesian Tertiary Hospital

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Abstract Content Routine pain score assessment is very important to assess the sufficiency of analgesics and sedatives in critically ill pediatric patients. Relevant instruments used may vary according to the age and indications. This study aimed to assess the sufficiency of analgesics and sedatives using several pain assessments scores among mechanically ventilated children in the PICU.

Methods This is a prospective cohort study. Children who underwent mechanical ventilation for 12 hours or more were included in the study. Exclusion criteria include patients admitted to the PICU after respiratory/cardiac arrest, patients on mechanical ventilation for 2 weeks or more, parents/guardians who sign do not resuscitate, patients with low chance of survival (palliative cases), and patients with neurologic deficit. COMFORT score, SBS, FLACC scale (for children aged 1-6 years old), and NVPS (for children aged 7 years and more) were recorded at hour-0, -6, -12, -18, and just before the patients were extubated.

Results A total of 42 subjects were recruited between October 2020 to August 2021. The mean age of the study participants were 61.7 (SD 13.7) months. The median COMFORT score in all 4 time points were within normal range (normal value 12-17), indicating good sedation and analgesia in our PICU with scoring during hour-0, -6. -12, -18, and during extubation day of 13 (8-18), 12 (8-16), 13.5 (8-19), 14 (8-20), and 15.5 (10-21) respectively. The median SBS value were -2 (-2 - -2), -1.5 (-2 - -1), -1.5 (-2 - -1), -1 (-2 - 0), -1.5 (-3 - 0), indicating that most patients were adequately sedated with ranging from responsive to noxious stimuli (-2) to gentle touch or voice (-1) with none of the patients were restless and agitated. The FLACC scale were mostly within mild discomfort classification (score 1-3) during the 4 time points were 2.5 (1-4), 2 (1-3), 3.5 (1-6), 3.5 (1-6), and 2 (0-4) while the NVPS were 0 (0-6), 1 (0-3), 1.5 (0-3), 0 (0-3), 0 (0-3) respectively, indicating no pain (score ≤2) in all time point.

Conclusion Most children in our PICU were adequately sedated and given proper analgetic mediation to prevent agitation. The COMFORT score, SBS, FLACC scale, and NVPS could be used in routinely in our PICU to assess sufficiency of analgesics and sedatives.

Key words COMFORT, SBS, FLACC, NVPS, sedation, analgesia, mechanical ventilation
Reference None

Category: 21. Pediatric Intensive & Critical Care 儿童危重症
1449

Incidence and Factors Associated with Ventilator-associated Events in Pediatric intensive care unit: A retrospective study in Chiangmai University Hospital

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Abstract Content Background:
Pediatric ventilator associated pneumonia (P-VAP) is associated with increased mortality and hospital morbidity. Patients with P-VAP were associated with a pre-existing pediatric ventilator associated event (P-VAE) and associated risk factors for the patients exposed. Therefore, we studied the incidence, consequences and risk factors associated P-VAE, P-VAP in pediatric intensive care unit in Chiang Mai university hospital.

Methods The retrospective study was performed including the pediatric patients 1 month - 18 years-old who were intubated for more than 48 hours in both pediatric intensive care unit (PICU) and pediatric cardiac intensive care unit (PCICU) between 1st July 2014 - 30th September 2020. We used the centers for disease control and prevention (CDC) P-VAE and P- VAP diagnostic criteria 2020.

Results One hundred and forty-eight episodes (median age 1.1 yrs (0.3-6.3 yrs), 58%male) were included. There were 49 P-VAE (33%) and 22 P-VAP (14.8%) patients, resulted for incidence of P-VAP and P-VAE 10.9 and 16.4 episode per 1,000 ventilator days, respectively. Univariate analysis the risks of P-VAE was done, including blood product transfusion, continuous enteral feeding, intermittent sedation, cuffed endotracheal tube, tracheostomy, history of reintubation, central line insertion, fluid overload percent in 72 hours on ICU admission, PRISMIII and PIM2 score. The risk factors associated to P-VAE were central line insertion (OR: 6.49; 95%CI: 1.29-32.67, p-value=0.023) and percent fluid overload in 72 hours of ICU admission (OR: 1.11; 95%CI: 1.04-1.18, p-value=0.002). Also, the mean of %FO in P-VAE and P-VAP patients were 9.24±6.54, 10.01±6.66, respectively. Subgroup analysis was done in both PICU and PCICU. The correlation analysis revealed that %FO in 72 hours was associated with P-VAE in both groups; correlation coefficient in PICU= 0.235 (P=0.040), and in PCICU 0.411 (P=0.001). The ROC curve analysis found that %FO ≥6.5 was the best cut-off value for predicting diagnosis of P-VAE which was 3.67 times greater than non P-VAE (95%CI: 1.76-7.69) with sensitivity 68% and specificity 63%. The consequences of P-VAE were increased in ICU length of stay (18 days (9.0 - 35.0), p-value=0.002), mechanical ventilator days (15.5 (8.0 - 32.0), p-value<0.001), and mortality rate (73%, p-value 0.003).
Conclusion The incidence of P-VAE and P-VAP presenting in the patient who had central line insertion and the main risk factor for P-VAE and P-VAP was presented in higher %FO. The consequence of P-VAE and P-VAP were increased PICU length of stay and duration of mechanical ventilation.

Key words Incidence; Central line insertion; % Fluid overload; Mechanical ventilation; Pediatric; Ventilator-associated event; Ventilator-associated pneumonia

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分类：21. Pediatric Intensive & Critical Care 儿童危重症
1480

Best evidence application of central venous catheter devices removal in the child's intensive care unit:a multi-center survey

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Objective The central venous catheter device (CVAD), also called the central venous catheter, is mainly used for clinical drug use, infusion and monitoring of blood flow mechanics status, blood sample collection and kidney replacement therapy. Indications for central venous catheter removal include catheter-related infections, persistent catheter blockages, catheter-related thrombosis, catheter damage, and end-of-treatment. The removal of the catheter from the internal jugular and subclavian central vein is a common clinical operation. Improper removal of the catheter may lead to air embolism, hematoma at the puncture site and rupture of the catheter. Therefore, this study implements best evidence application of central venous catheter removal in the intensive care unit of 6 tertiary children hospitals in China to reduce the complications associated with central venous catheter removal.
Methods Following the clinical evidence practice and application mode of JBI evidence-based Care Center, literature related to children's central venous catheter removal was retrieved through evidence-based database system, and the best evidences were collected. In the clinical transformation of best evidence, i-PARIHS evidence-based practice conceptual framework is used for barrier analysis and action plan development.
Results
Results Finally, 6 central venous extubation related evidences were retrieved through retrieval:1.The patient should lay fat during CVAD removal to avoid an air embolus. (Grade B) 2.The platelet count should be more than 50 × 109/l and the INR less than 1.5 before catheter removal. (Grade B) 3.The patient should be instructed to perform the Valsalva maneuver or hold their breath during catheter removal to prevent air embolism. (Grade B) 4.The catheter should be inspected carefully after removal to ensure it is intact. (Grade B) 5.If removed for suspected infection the catheter tip should be sent to the laboratory for culture. (Grade B) 6.Firm, digital pressure is applied for at 5 minutes followed by application of an occlusive dressing. (Grade B).The total number of cases included in the baseline survey and the one-round evidence review of the central venous catheterization was 45 and 31 respectively, and the total number of review indicators in the baseline survey and the one-round evidence review was 238 and 173. Through the analysis of obstacle factors, formulate the SOP of CVC extubation, conduct CVC extubation maintenance homogeneity training for general nursing staff, conduct CVC maintenance qualification certification for nursing staff, and shoot CVC extubation videos. Evidence-based evidence application compliance in baseline investigations and a round of evidence review center venous catheter removal improved significantly overall (P<0.01). During extubation, the position management, coagulation function examination, prevention of air embolism and Valsavala movement were significantly improved (P<0 .01). Compliance of two of evidences, that inspection of catheter intact after each extubation and if removed for suspected infection the catheter tip should be sent to the laboratory for culture, were high at baseline and round of review, with no statistically significant difference.

Conclusion Applying the best evidence of central venous catheter removal to clinical practice can standardize nurse behavior, improve nurse's evidence-based compliance, and reduce the incidence of complications associated with central intravenous tube removal.

关键字 central venous catheter, catheter removal, multi-center, best evidence

分类：21. Pediatric Intensive & Critical Care 儿童危重症
1485

The status of early rehabilitation nursing of children in pediatric intensive care unit:a cross-sectional study

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Objective With the development of critical care medicine, the mortality of children with severe illness has decreased significantly, and a large proportion of critically ill children who survived still have physical dysfunction for several years after discharge. Early rehabilitation can significantly increase the activity ability of patients out of ICU, reduce the length of hospitalization and mechanical ventilation, reduce the mortality of patients in hospital, reduce the occurrence and progression of post-intensive care syndrome and ICU acquired weakness, improve the prognosis, and promote the recovery of critically ill children. In this study, we investigate the status quo of early rehabilitation nursing and the cognition and attitude of nursing staff to early rehabilitation in PICU of tertiary children hospitals, analyze and evaluate influencing factors and countermeasures of early rehabilitation. The objective of this study is to provide theoretical basis for exploring comprehensive intervention measures for early rehabilitation of critically ill children.

Methods Convenient sampling was adopted to select PICU specialist nurses from 22 children's tertiary hospitals in China as the survey objects. The status quo and influencing factors of early rehabilitation nursing were investigated by using a self-compiled questionnaire of early rehabilitationt, Cronbach's α=0.961. In addition, the questionnaire was set up as an electronic questionnaire, and the link website and two-dimensional code of the questionnaire were issued to the respondents through wechat and email, and the upper limit of each IP address was set to one time.

Results A total of 683 valid questionnaires (97.4%) were collected. Nurses under 30 years old, with less than 5 years of service and at primary level have higher cognition and attitude towards the early rehabilitation of critically ill children. Awareness of the importance of early rehabilitation for critically ill children (P=0.007) and rehabilitation related training (P=0.002) can promote the development of early rehabilitation for critically ill children. Status of early rehabilitation of children with PICU in China: 28.84% have carried out early rehabilitation treatment. In the early rehabilitation departments that have carried out early rehabilitation, more than 80% have carried out early activities such as posture sputum discharge, swallowing function training and bladder function exercise. 33.81% used rehabilitation apparatus. 24.87% used rehabilitation assessment tools to assess the effect of rehabilitation. Nutritional status and cognition of children with PICU, inadequate early rehabilitation training, safety of treatment and limitation of early rehabilitation treatment personnel are the main obstacles in the implementation of PICU rehabilitation care. **Conclusion** The rehabilitation of critically ill patients is getting more and more attention, but the early rehabilitation of critically ill children is still in its infancy. At present, the early rehabilitation nursing of PICU in China has not been spread out and is still at a low level. Nursing staff lack professional knowledge of rehabilitation, and there is a large variation between clinical practice behaviors. There is a lack of standardized system, which needs to be further improved. Therefore, it is necessary to build evidence-based early

rehabilitation nursing programs according to China's national conditions, promote multidisciplinary cooperation, standardize early rehabilitation behavior of critically ill children, improve prognosis of children, and reduce the burden on families and society. Rational allocation of medical human resources, strengthen the concept of early rehabilitation of critically ill children, train medical staff in early rehabilitation techniques, and establish a multidisciplinary rehabilitation team of PICU to promote the development of early rehabilitation of critically ill children.

关键字 Pediatric intensive care unit, early rehabilitation, multi-center investigation

分类：21. Pediatric Intensive & Critical Care 儿童危重症
1494

The best evidence for the application of central venous catheter maintenance in critically ill children

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Objective:Central Venous Access Devices (CVADs) has been widely used in the rescue of critically ill children, and has become the main intravenous infusion pathway for the infusion of vasoactive drugs, chemotherapy drugs, intravenous hypernutrition and other high-risk drugs in critically ill children.Central line-associated bloodstream infections (CLABSI) and sepsis are major complications of CVADs, which significantly increase infant and child morbidity and mortality.Therefore, how to effectively prevent central venous catheter-related bloodstream infection is extremely important.In this paper, the best evidence of central Venous catheter (CVC) maintenance will be applied to clinical practice based on the clinical evidence application model, so as to improve nurses' compliance with the application of practical evidence, thus reducing the incidence of central venous catheter associated bloodstream infection (CLABSI).**Method** :Follow the clinical evidence practice and application mode of JBI Evidence-based Care Center, including evidence acquisition, status review, evidence introduction and effect evaluation.In the evidence acquisition process, PIPOST was constructed according to clinical problems, evidence was retrieved, evidence quality was evaluated and evidence summary was formed;In the status review process, 19 pieces of evidence summarized by system retrieval were converted into 22 clinical review indicators. A certain sample size was selected to conduct baseline review in PICU of a Grade A Children's Hospital in Shenzhen city to understand the compliance of nursing center venous maintenance behavior to evidence-based review standards.In the evidence introduction stage, the i-PARIHS evidence-based practice conceptual framework is adopted to analyze the obstacle factors from the three levels of change, change recipients and organizational environment and construct targeted action strategies.The effect evaluation process evaluates the impact of evidence transformation on the system, practitioners and patients from three levels: process, result and structure.
Result :Evidence transformation time was from September 2019 to April 2020. A total of 109 children with catheterization and 53 nurses were included, and 842 clinical reviews were conducted.Before and after the application of evidence, the score of nurses on evidence-based CVC maintenance knowledge increased from 67.94+13.01 to 67.94+13.01, and the difference was statistically significant (P<0.01) .8 audit standards with poor compliance with evidence were significantly improved (P<0.05) .For catheter extraction, there were fewer clinical reviews, and the evidence-based compliance of criteria 17, 18, 21 and 22 was improved (P<0.05) ,There were no bleeding at puncture point, air embolism, incomplete central venous catheter after extubation in all children.The central venous catheter-related bloodstream infection rate decreased from 1.27‰ to 0.78‰ (P<0.05).
Conclusions: Applying the best evidence of central venous catheter maintenance to clinical practice can standardize nurses' behavior, improve nurses' compliance with evidence, and effectively promote continuous quality improvement of nursing.22 evidence-based practice standards for central venous catheter maintenance can effectively reduce the rate of infection associated with central venous catheters,Save the patient's economic cost.At present, more and more children in the PICU are implanted with central venous catheter and then transferred to the

other wards. In order to effectively avoid the risk of complications after extubation, it is necessary to carry out evidence-based nursing practice of central venous catheter extubation in the whole hospital.

关键字 Catheter-Related Infections, Central Venous Catheters, critically ill children Evidence-Based Practice

分类：21. Pediatric Intensive & Critical Care 儿童危重症
1507

Post-intensive care syndrome in children: A concept analysis

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We aimed to clarify the concept of post-intensive care syndrome in the pediatric population (PICS-p). The Walker and Avant's strategy for concept analysis was employed. The literature was searched using the following keywords: "post-intensive care syndrome," "PICU," "children," and "concept analysis." PICS-p is characterized by new or worsening impairments in the physical, cognitive, or mental health status arising after critical illness. These impairments "persist beyond acute care hospitalization." The occurrence of PICS-p can significantly affect the patients' quality of life and daily activities, increases the risk for treatment complications and memory impairment, and adds stress to the family. Our findings provide insight into PICS-p and opens new avenues for research and interventions. The definition of PICS-p presented in this article can be used by nurses to promote symptom management. Further research is needed to determine the relationships between the antecedents, attributes, and consequences of PICS-p and to develop effective interventions.

关键字 pediatric intensive care unit, post-intensive care syndrome, pediatric, concept analysis

分类：21. Pediatric Intensive & Critical Care 儿童危重症
1690

The Impact of Overweight and Obesity on Sepsis Mortality Among Children 28 Days to 5 Years of Age in Pediatric Intensive Care Unit

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Objective To explore the impact of overweight and obesity on sepsis mortality among children 28 days to 5 years of age in pediatric intensive care unit (PICU).
Methods Data of all patients between 28 days and 5 years of age admitted to the PICU of Children's Hospital of Chongqing Medical University from January 1, 2013 to June 1, 2020 with a diagnosis of sepsis, severe sepsis or septic shock were retrospectively collected. The weight for height/length Z score was used to evaluate patients' weight status. According to the hospital mortality, patients were divided as survivors and nonsurvivors. We performed bivariable analysis and logistic regression to determine the association between overweight/obesity and hospital mortality.
Results 264 patients (median age, 8.0 months; male, 57.2%; median weight for height/length Z score, 0.3) were enrolled in the final study. 30 (11.4%) patients were overweight or obesity. There were significant differences among the gender and the serum creatinine level between overweight/obese and normal patients. Hospital mortality was 18.9%. Bivariable analysis shows that the weight for height/length Z score(P=0.035), with a diagnosis of septic shock(P<0.001), PELOD-2 score(P<0.001), PRISM III(P<0.001), arterial blood lactate(P<0.001), use of vasoactive drugs(P<0.001), use of invasive mechanical ventilation(P<0.001) and the number of organ dysfunction(P<0.001) were significantly different between survivors and nonsurvivors. There was no difference in mortality for overweight/obese patients compared to normal patients no matter adjusted for other factors or not. However, higher weight for height/length Z score may be a protective factor of hospital mortality (OR 0.703 [95%CI 0.516-0.959], P<0.026).
Conclusion Hospital mortality was similar for overweight/obese patients and normal patients among children 28 days to 5 years of age with sepsis, but higher weight for height/length Z score may be a protective factor of hospital mortality.

关键字 Sepsis; Obesity; Overweight; Mortality

分类：21. Pediatric Intensive & Critical Care 儿童危重症
1702

Glycemic Variability is Independently Associated with Poor Prognosis in Main PICU Centers in Southwest China

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Background: Glucose variability (GV) is one of the common complications in critically ill patients, and studies investigating the role of GV in the prognosis of pediatric patients are scarce in China. And there is no consensus on the measurement of GV. So this study took a prospective, multi-center cohort observational study to identify the 'best' index of variability in non-diabetic critically ill children and to confirm whether GV is associated with unfavorable outcomes and whether this association persists after control of hypoglycemia and hyperglycemia.
Design: A prospective, observational, and multicenter study.
Setting: Five PICUs in Southwest China.
Materials and Methods: Four GV indices were chosen and calculated in our study, namely, mean absolute glucose (MAG), standard deviation (SD), glycemic lability index (GLI), and another metric-average consecutive absolute change percentage (ACACP), which can be used in the real-time clinical decision. The primary outcome was 28-day mortality. Multivariate Cox regression analysis was used to identify the potential predictors for the outcome. And the area under the curve (AUC), net reclassification improvement (NRI), and integrated discrimination improvement (IDI) were calculated to assess the predictability of dysglycemia (glucose variability and hypo/hyperglycemia) on the unfavorable outcome.
Results: Of the total of 780 participants, 12.4% (n=97) died within 28 days after PICU admission. There were statistical differences in terms of four GV indices (SD, GLI, MAG, and ACACP) between survivors and non-survivors, in which MAG obtained the largest area under the curve and showed a strong connection to ICU mortality independently. Subsequent addition of MAG to the multivariate Cox model for hyperglycemia resulted in further quantitative evolution of the model statistics (AUC 0.651 to 0.681, P=0.001; IDI: 0.017, P=0.044; NRI:0.224, P=0.186). And the impact of hyperglycemia (adjusted HR1.419, 95% CI 0.815-2.471, p=0.216) on outcome was attenuated and no longer statistically relevant after adjustment for MAG (adjusted HR 2.455, 95%CI 1.411-4.270, p=0.001).
Conclusions: This report is the first multicenter prospective study of pediatric dysglycemia conducted in Southwest China. And the results attempt to endorse and expand on previous literature findings by showing that fluctuation in glucose control affects clinical prognosis negatively in PICU children and glucose variability may be more strongly associated with mortality rates, compared with hypoglycemia and hyperglycemia. These findings emphasize the crucial role of GV in PICU children. GV index that contains information such as time, rate of change, etc. is the focus of future research. MAG may be a good choice.

关键字 dysglycemia, glycemic variability, MAG, pediatrics, critically ill, mortality.

分类：21. Pediatric Intensive & Critical Care 儿童危重症
1708

Epidemiology of Cardiopulmonary Arrest and Outcome of Resuscitation in PICU Across China: A Prospective Multicenter Cohort Study

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Background: To investigate the epidemiology and resuscitation effects of cardiopulmonary arrest among critical ill children and adolescents during PICU stay across China.

Methods: A prospective multicenter study was conducted in 11 PICUs in tertiary hospitals. Critical ill children aged from 1 month to 18 years with cardiopulmonary arrest, received cardiopulmonary resuscitation (CPR) and consecutively hospitalized in PICU during their study period (December 1st, 2017 to October 31st, 2018) were enrolled. Data was collected and analyzed using the "in-hospital Utstein style". Neurological outcome was assessed with the pediatric cerebral performance category among children who survived.

Results: Total of 372 children among 11588 cases (3.2%) in PICU had cardiopulmonary arrest during PICU stay with 281 (75.5%) received CPR and 24.5% required “Do Not Resuscitation”. Cardiopulmonary disease was the most common reason for cardiopulmonary arrest, with respiratory system 27.8% and circulatory system 19.6%. The most frequent initial heart rhythm was bradycardia (79%). About 170 (60.3%) of children had recovery of spontaneous circulation, 91 (37.4%) cases survived to hospital discharge, 28 (11.5%) cases survived 6 months after discharge and 19 (7.8%) survived 1 year after discharge. Among the 91 children who remained alive when discharge, 47.2% got a good PCPC score (1-3). The results of regression analysis revealed that CPR duration, epinephrine frequency correlated with ROSC, while CPR duration, original diseases, CPR times, ventricular tachycardia/ventricular fibrillation, epinephrine frequency was associated with survival to discharge to hospital.

Conclusion: The prevalence of cardiopulmonary arrest in critical ill children and adolescent is relatively high. The long-term result of children and adolescents survived cardiopulmonary resuscitation is good. CPR duration and frequency of epinephrine use are independent factors for the effect of cardiopulmonary resuscitation.

关键字 心跳呼吸骤停，心肺复苏，PICU，前瞻性多中心研究，

分类：21. Pediatric Intensive & Critical Care 儿童危重症
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Long-term safety of moxifloxacin in children with severe macrolide-resistant Mycoplasma pneumoniae pneumonia

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Background：With the increased macrolide-resistance rate of Mycoplasma pneumoniae, searching of alternative medicine is important. Moxifloxacin is not approved by China and US Food and Drug Administration for pediatric use because of its potential to cause collagen-associated adverse events (AEs). Although its use might be indicated when treating Mycoplasma pneumonia, data of its safety and tolerability in pediatric patients are limited. The primary objective of this study was to evaluate the safety and tolerability of systemic moxifloxacin therapy in children with severe Mycoplasma pneumoniae pneumonia (SMPP).
Methods：We conducted an observational study of SMPP patients aged <18 years at pediatric intensive care unit between January 2017 and May 2020. The patients were divided into two groups according to whether using intravenous moxifloxacin (10mg/kg, qd) . Patients' demographics, clinical characteristics, imaging data, duration for moxifloxacin were extracted via chart review. The data about AEs after using moxifloxacin at least 1 year were collected through internet or clinic visits. The possible attributable AEs of moxifloxacin was decided on final conclusion from the pediatric critical care specialist, rheumatologist, orthopedist, pharmacist and radiologist.
Results：Data of patients were recruited from pediatric intensive care unit in Beijing Children's Hospital: 23 patients were divided into moxifloxacin group and 7 into control group. Among patients in moxifloxacin group with the average follow-up time 2.4 years, 30.43% (7/23) of them had regular mild knee pain, 21.74%(5/23) had heart valve regurgitation and 96.00%(24/25) had normal knee radiographs. The abnormal knee radiograph which indicated hydrops articuli was not associated with moxifloxacin. Besides，in patients of the control group with the average follow-up time 4.2 years, 28.57% (2/7) had regular mild knee pain, 14.29%(1/7) had heart valve regurgitation and 100.00%(25/25) had normal knee radiographs. Patients in both groups had normal weight-bearing joint function based on weight-bearing joint score scales.
Conclusions： Moxifloxacin was well tolerated and safety in treating SMPP in children with dose of 10mg/kg/d and there was no correlation between AEs and moxifloxacin.

关键字 moxifloxacin; severe Mycoplasma pneumoniae pneumonia; macrolide-resistance; children; safety

分类：21. Pediatric Intensive & Critical Care 儿童危重症
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The value of satellite culture in PICU sterile humoral culture was assessed

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Severe infections are a common cause of death in children with PICU,sterile humoral culture is the "gold standard" for diagnose infection,the collected body fluid specimens shall be submitted for inspection as soon as possible.However,during the laboratory closing time,specimens collected by PICU night shift must be placed until the laboratory is open.In November 2018, our department enabled the satellite culture,specimens collected by PICU night shift can be cultured immediately.This article was designed to analyze the culture data of PICU sterile humoral specimens from January 2017 to October 2018 and January 2019 to December 2020,thus assessing the value of satellite cultures in PICU sterile humoral culture.

Background:The value of satellite culture in PICU sterile humoral culture was assessed.

Method: Sterile humoral samples from the laboratory from January 2017 to October 2018 were collected as control groups(LAB group),sterile humoral samples grown with satellite cultures were used as the test group(PICU group) from January 2019 to December 2020,comparing differences in positive test times and positive rates between PICU group and LAB group,the p-values were calculated by using a t-test for two independent samples.What's,more,counting the positive detection time of sterile humoral specimens in 2017 and 2020, and analyzing their distribution rules.

Results:
The sterile humoral samples from 4634 PICU patients were analyzed in Table 1, including PICU group was 2099 and LAB group was 2535.Of these, 132 specimens tested positive,there were 70 cases in PICU group, positive rate of 3.33%.And 62 cases in LAB group,positive rate of 2.45%.The positive mean test time PICU group was 12h8min shorter than the LAB group ($p < 0.01$).

Figure 1 analyzes 688 sterile humoral samples from patients with PICU in 2020,statistics of the starting culture time distribution for 24h samples, we can see it,the number of samples from the starting culture time for the night shift (18:00-8:00) was 417, accounting for 60.62%,the starting culture time was a white shift (8:00-17:00) with 271 samples, accounting for 39.38%,specimens were collected and cultured at each time of the day.

Conclusions:Comparing to no satellite cultures used before November 2018,the positive rate was increased, and the average positive test time was shortened.The increase in the positive rate may be related to the number of double bottles and the shortened time of sampling to the boarding machine,it will require further research and analysis.What's more,the shortening of the positive test time can win time for severe children to adjust antibiotics as soon as possible.In general, the application of satellite culture realizes the machine as soon as possible to shorten the time of positive detection,and escort children with severe infection.

关键字 PICU,satellite culture,infection

分类：21. Pediatric Intensive & Critical Care 儿童危重症
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Blood purification technology was applied to treat type Ia glycogen storage disease complicated with severe lactic acidosis and the related literature review

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Objective:Glycogen storage disease type Ia is a genetic disease caused by glucose-6-phosphatase deficiency.Severe lactic acidosis is a serious complication of glycogen storage disease type Ia. This article aims to analysis the clinical features and the treatment of glycogen storage disease type Ia with severe lactic acidosis.Methods:We carried out a retrospective analysis of the diagnosis and treatment of a patient with glycogen storage disease type Ia with severe lactic acidosis during the COVID-19 period and the review related literature.Results:The child was admitted to our hospital for ″chest pain and vomiting for 3 days, aggravated with dyspnea for 5 hours″.The child had a history of type Ia glycogen storage disease.After admission,arterial blood gas analysis PH:7.192, lactic acid:26.77mmol/L.Above all,the child was diagnosed with type Ia glycogen storage disease combined with severe lactic acidosis.After 4 hours of hemodialysis and 36 hours of continuous blood purification,retesting arterial blood gas biochemistry indicated PH:7.482, lactic acid: 7.41mmol/L, blood glucose:10.7mmol/L.Conclusion:Continuous renal replacement therapy is an effective treatment for severe lactic acidosis.While preventing and controlling during the COVID-19 period,attention should be paid to the treatment of special populations such as glycogen storage to prevent serious complications.

关键字 glycogen storage disease lactic acidosis continuous renal replacement therapy

Hematology & Oncology

血液与肿瘤

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Integrated bioinformatics analysis of hub gene and key module in MLL-r acute lymphoblastic leukemia

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Abstract Content Despite much improvement in the treatment for acute lymphoblastic leukemia (ALL), childhood ALL with MLL-rearrangement (MLL-r) still has poor dismal prognosis attributed to hyperleukocytosis, aggressive form with early relapse, and central nervous system involvement. Thus, defining mechanisms underlying MLL-r ALL maintenance is critical for developing effective therapy.

Methods Two GEO datasets were identified via the Oncomine website. Differentially expressed genes (DEGs) between MLL-r ALL and non MLL-r ALL were analyzed by R software. GO function and KEGG pathway analysis of DEGs was carried out via DAVID online analysis tool. We also built protein-protein interaction network and used Cytoscape to calculate the top 40 DEGs and the pathways they were involved in. Gene Set Enrichment Analysis systematically defined all the gene expression data. Weighted Gene Co-expression Network Analysis was used to identify the key gene modules and hub genes associated with leukemia. In addition, we used the UCSC Xena browser to detect the hub genes expression data of Therapeutically Applicable Research to Generate Effective Treatments program. Quantitative real-time PCR was also conducted for hub genes expression in our patients samples and cell lines.

Results GSE13159 and GSE28497 were analyzed using R software and a total of 1045 DEGs were identified, 301 of which were up-regulated while 744 were down-regulated. The up-regulated DEGs were mainly enriched in B cell proliferation and transcriptional misregulation in cancer pathway. Eighteen hub genes highly associated with leukemia traits were observed by combining DEGs and the key module found by WGCNA. A total of 9 hub genes expression were found highly corelated with MLL status. High expression of 9 hub genes were also observed in RS4;11 (MLL-AF4 ALL) compared to the RCH-ACV (non MLL-r ALL). Further, we demonstrated that 3 hub genes including BCL11A, GLT8D1 and NCBP2 had significantly higher expression in MLL-r ALL patients than that in the non MLL-r ALL patients.

Conclusion These findings suggest that BCL11A, GLT8D1, and NCBP2 are correlated with the MLL status of childhood ALL. Childhood ALL patients with higher hub gene expression are subject to positive MLL status. Further study is required to elucidate the role of these three genes in the development of MLL-r ALL.

Key words acute lymphoblastic leukemia, MLL rearrangement, bioinformatics, differentially expressed genes

Reference

分类：12. HaematologyOncology 血液与肿瘤
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Clinical Study Of MAP2K1-mutated Langerhans Cell Histiocytosis In Children

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Background: Langerhans cell histiocytosis (LCH) is a rare clonal and hematologic disease, mainly occurring in children, characterized by the expansion of Langerhans cells derived from myeloid precursors. MAP2K1 is another common mutant gene in LCH besides BRAFV600E mutation. However, the clinical features of children with MAP2K1-mutated LCH is still unclear.

Methods: Next-generation sequencing of whole exomes was used to detect mutations in the MAPK pathway. The clinical data of newly treated patients with MAP2K1-mutated LCH in Beijing Children's Hospital, Capital Medical University from July 2017 to October 2020 were collected. At the same time, two control groups were enrolled, consisting of all newly treated patients who had either the BRAFV600E mutation (n=133) or no known mutation of the MAPK pathway (n=59). Each evaluation was conducted according to the Histiocyte Society Evaluation and Treatment Guidelines (2009). Follow-up was continued until December 1, 2020, or until the patient died.

Results: We found 13 mutations of the MAP2K1 gene, which were mainly concentrated at p.53-62 and p.98-103. The most common mutation site was c.172_186del (12/37). The male-to-female ratio of the 37 patients with a MAP2K1 mutation was 1.31:1, and the median age at disease onset was 4.56 (1.54, 9.42) years old. The median follow-up time was 17.67 (4.82, 24.92) months. Compared with the BRAFV600E mutation group, the patients with MAP2K1 mutations were mainly characterized by single system multiple bone involvement (P=0.022), with later disease onset (P=0.029) as well as less involvement of skin (P=0.002) and risk organs, especially liver (P=0.024). The levels of C-reactive protein (CRP), IFN-γ, IL-10 and IL-6 in the MAP2K1 mutation group were significantly lower (P<0.05). There was no significant difference in clinical features and laboratory examinations compared with the no known mutation group. Except for the patient who was not evaluated at the 6th week as planned, the ORR was 48.6% (17/35), and the DCR was 85.7% (30/35) after 6 weeks of first-line chemotherapy. There was no significant difference in ORR and DCR after 6 weeks of first-line chemotherapy among the three groups (P>0.05). The 2-year progression-free survival (PFS) rate of first-line treatment in MAP2K1-mutated patients was 65.6% ± 9.5%, without a significant difference among the three groups. In terms of the efficacy of second-line chemotherapy, there was no significant difference in 2-year PFS between the MAP2K1 mutation group and the BRAFV600E mutation group, but the PFS of both groups were significantly lower than that of the no known mutation of the MAPK pathway group ($\chi 2=6.531$, P=0.011; $\chi 2=7.409$, P=0.006; log-rank test. We compared the clinical and laboratory characteristics between different mutated domains and found that there was no significant difference in clinical features (including age, sex, and organs involved), laboratory examinations and prognosis (P>0.05). The prognosis of patients with lung involvement was poor [HR (95% CI) = 6.312 (1.769-22.526), P = 0.005]. More progression or relapses could be found in patients with bony thorax involvement (8/17 vs. 2/20, P=0.023), yet

involvements in craniofacial bone (8/26 vs. 2/11, P=0.688) and limb bone (5/12 vs. 5/25, P=0.240) were not correlated to disease progression or relapse. Conclusions: MAP2K1 mutations in pediatric LCH are concentrated at amino acids 53-62 and 98-103, and c.172_186del is the most common mutation site. Compared with patients with the BRAFV600E mutation, patients with the MAP2K1 mutation were mainly characterized by more SS-multiple bone involvement, less RO and skin involvement and later disease onset, requiring clinical stratification and precise treatment. The prognosis of patients with lung involvement, frequently associated with bony thorax involvement, is poor and should be given more attention in further studies.

关键字 MAP2K1; Mutation; Langerhans Cell Histiocytosis; Children

分类：12. HaematologyOncology 血液与肿瘤
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Purple sweet potato anthocyanins elicit calcium overload-induced cell death by inhibiting the calcium-binding protein S100A4 in acute lymphoblastic leukemia

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This study aimed to evaluate the effects of purple sweet potato anthocyanins (PSPAs) on acute lymphoblastic leukemia (ALL) cells to elucidate the molecular mechanism underlying the anticancer properties of PSPAs. The results showed that PSPAs significantly suppressed cell proliferation by inducing obvious G2/M phase arrest. In addition, PSPAs dramatically increased the intracellular Ca2+ levels, thereby leading to calcium overloadinduced cell death. Furthermore, to evaluate the relevant mechanism, bioinformatic, subcellular localization,molecular docking, and Western blot analyses were performed. PSPAs induced calcium overload by inhibiting the protein expression of S100A4. An additional assay combining S100A4 induction and PSPA treatment reconfirmed that S100A4 was the potential target of PSPAs and that PSPAs mainly exerted their antileukemic effects through the p38/c-Myc/CDK1-Cyclin B axis. Our findings indicate that PSPAs are promising therapeuticagents for ALL.

关键字 Purple sweet potato; Anthocyanin ; Acute lymphoblastic leukemia; Calcium overload; S100A4

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A recombinant Chinese measles virus vaccine strain rMV-Hu191 inhibits human colorectal cancer growth through inducing autophagy and apoptosis regulating by PI3K/AKT pathway

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Background: Colorectal cancer, a highly malignant tumor of the digestive system, is the fourth lethal malignancies worldwide due to its high mortality, and also has a high incidence in children. With the applications of conventional therapies such as surgery, adjuvant chemotherapy and radiotherapy, colorectal cancer could recur frequently after the initial treatment or even entire removal of the tumor. It is reported that the mean survival time of the CRC is still less than 3 years. Thus, effective and promising therapeutic strategies are still urgently needed across the globe. The potential therapeutic effect of oncolytic measles virus therapy has been demonstrated against many malignancies. However, the oncolytic effect of the recombinant Chinese measles virus vaccine strain rMV-Hu191 on human colorectal cancer and its mechanism remain unknown. In this research, we have elaborated for the first time that rMV-Hu191 generated effectively oncolytic effects in human CRC both in vitro and in vivo.

Method: Cell proliferation and cell apoptosis were evaluated by CCK-8 assay and flow cytometry, respectively. The expression levels of apoptosis and autophagy-related proteins were detected by Western blot assay. And the formation of autophagosomes was detected by transmission electron microscopy. Apoptosis inhibitor Z-VAD, autophagy promoter RAPA, autophagy inhibitor CQ and shATG7 were used to regulate apoptosis and autophagy, respectively. Mice bearing human colorectal cancer xenografts were used to confirm the tumor inhibition effects in vivo.

Results: Our data demonstrated that recombinant Chinese measles virus vaccine strain rMV-Hu191 generated tumor therapeutic efficacy in human CRC both in vitro and in vivo. rMV-Hu191 induced caspase-dependent apoptosis and complete autophagy, and activated the PI3K/AKT pathway. And autophagy served as a protective role in rMV-Hu191-induced apoptosis. PI3K/AKT pathway regulated this two processes by promoting rMV-Hu191-induced autophagy and inhibiting rMV-Hu191-induced apoptosis. Taken together, in this study, we well explain the relationship between rMV-Hu191-induced apoptosis, autophagy and the PI3K/AKT pathway.

Conclusions: In conclusion, we demonstrate for the first time that rMV-Hu191 is a candidate for oncolytic virus therapy in human colorectal cancer. In this study, we well explained the relationship between rMV-Hu191-induced apoptosis, autophagy and PI3K/AKT pathway. The mechanism may provide a theoretical basis for the application of this attenuated measles virus as a novel oncolytic agent in the treatment of human colorectal cancer, such as combinational therapy of rMV-Hu191 with agents targeting autophagy or PI3K/AKT pathway.

关键字 Colorectal cancer, Oncolytic measles virotherapy, Apoptosis, Autophagy, PI3K/AKT signaling pathway

分类：12. HaematologyOncology 血液与肿瘤
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Synergism of rMV-Hu191 with cisplatin to treat gastric cancer by acid sphingomyelinase mediated apoptosis requiring integrity of lipid raft microdomains

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Background
DDP-based chemotherapy is one of the first-line treatment in GC. However, the therapeutic efficacy of DDP is limited due to side effects. Therefore, it is of great significance to develop novel adjuvants to synergize with DDP. We had demonstrated previously that rMV-Hu191 had antitumor activity in GC. Here we examined the synergism of rMV-Hu191 with DDP in vitro and in vivo.
Methods
Cellular proliferation, the synergistic effect and cell apoptosis were evaluated by CCK-8 assay, ZIP analysis and flow cytometry respectively. The protein levels and location of ASMase were monitored by western blot and immunofluorescence assay. shRNA and imipramine were used to regulate the expression and activity of ASMase. MβCD was administrated to disrupt lipid rafts. Mice bearing GC xenografts were used to confirm the synergism in vivo.
Results
From our data, combinational therapy demonstrated synergistic cytotoxicity both in resistant GC cell lines from a Chinese patient and drug-nonresistant GC cell lines, and increased cell apoptosis, instead of viral replication. Integrity of lipid rafts and ASMase were required for rMV-Hu191 and combination induced apoptosis. The ASMase was delivered to the lipid raft microdomains at the initial stage of rMV-Hu191 treatment. In vivo GC mice xenografts confirmed the synergism of combinational treatment, together with increased apoptosis and trivial side-effects.
Conclusions
This is the first study to demonstrate that rMV-Hu191 combined with DDP could be used as a potential therapeutic strategy in GC treatment and the ASMase and the integrity of lipid rafts are required for the synergistic effects.

关键字 Gastric cancer; Recombinant Chinese Hu191 measles virus; Cisplatin; ASMase; Lipid rafts

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Hinokiflavone induces apoptosis, cell cycle arrest and autophagy in chronic myeloid leukemia cells through MAPK/NF-κB signaling pathway

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Abstract: **Background** Chronic myeloid leukemia (CML) is a myeloproliferative tumor originating from hematopoietic stem cells, and resistance to tyrosine kinase inhibitors (TKI) has become a major cause of treatment failure. Alternative drug therapy is one of the important ways to overcome TKI resistance. Hinokiflavone (HF) is a C-O-C type biflavonoid with low toxicity and antitumor activity. This study investigated the antitumor effect and possible mechanisms of HF in CML cells. **Method** Cell viability was measured by CCK-8 assay. Cell apoptosis and cell cycle distribution were analyzed by flow cytometry. Western blotting was used to assess protein expression levels. **Results** HF significantly inhibited the viability of K562 cells in a concentration- and time-dependent manner and induced G2/M phase arrest by up-regulating p21 and down-regulating Cdc2 protein. Furthermore, HF induced caspase-dependent apoptosis by activating JNK/p38 MAPK signaling pathway and inhibiting NF-κB activity. In addition, HF induced autophagy by increasing LC3-II expression and p62 degradation. **Conclusions** HF induces apoptosis, cell cycle arrest and autophagy in chronic myeloid leukemia cells through MAPK/NF-κB signaling pathway. HF shows a good anti-leukemia effect and is expected to become a potential therapeutic drug for CML.

关键字 Keywords: Hinokiflavone; Chronic myeloid leukemia; MAPK; NF-κB; Apoptosis; Autophagy

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Crizotinib in treatment of inflammatory myofibroblastic tumor in children with positive ALK gene:A report of 4 cases

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Objective To investigate the efficacy and safety of crizotinib in the targeted treatment of ALK gene positive inflammatory myofibroblastic tumor in children.
Methods Four children with ALK gene positive inflammatory myofibroblastic tumor admitted from January 2019 to June 2021 were retrospectively analyzed. The ratio of male to female was 3:1, the age ranged from 5 years to 11 years, and the median age was 8 years and 5 months. Four children received Crizotinib (280mg/m2, Q12h), clinical observation of the efficacy and adverse drug reactions. Regular ultrasonography or enhanced CT examination of primary tumor site was performed in outpatient or inpatient department to observe the curative effect. Meanwhile, blood routine examination, liver and kidney function, myocardial enzyme spectrum, electrocardiogram, cardiac function, hearing and vision examination were performed.
Results Four children with inflammatory myofibroblastic tumor originated from abdominal cavity and unilateral orbit, respectively. Immunohistochemistry and FISH were positive for ALK gene. Four patients responded well to crizotinib treatment, and all survived after 10-30 months of follow-up. After partial resection or biopsy, 3 children began to take crizotinib orally, and all of them had complete response about 2 months later, and continued to take crizotinib orally. Another patient with abdominal tumor underwent complete resection and received crizotinib orally for 12 months was in complete remission. The patient relapsed 1 month after trial withdrawal, and was reoperated and continued to take crizotinib orally for 7 months. At present, the patient is in complete remission. In 2 cases, Q-T interval of ecg was prolonged during the treatment of crizotinib, which could be recovered after temporary withdrawal of medication, but no abnormal ECG was found after continued medication. None of the children had abnormal blood, liver and kidney function, myocardial enzyme spectrum, cardiac function, hearing and vision.
Conclusion Surgical resection is the main treatment for inflammatory myofibroblastic tumor, which is insensitive to radiotherapy and chemotherapy and prone to recurrence. For cases with incomplete resection, there is no standard treatment strategy at present. Chemical evidence of curative effect is limited, the sarcoma network working group guidelines recommend adriamycin alone as a treatment of choice, or doxorubicin combined chemotherapy regimens of ifosfamide try or curative effect can be obtained at home and abroad, but the center reported efficacy not sure, most cases of surgery and chemotherapy is also repeated recurrence, Therefore, targeted therapy in addition to surgery and chemotherapy has become a new direction for the treatment of inflammatory myofibroblastic tumor. Crizotinib is a potent inhibitor of ALK. In this study, crizotinib treated 4 children with ALK gene positive inflammatory myofibroblastic tumor with positive clinical efficacy, which can be used as preoperative treatment for tumor shrinkage and postoperative consolidation therapy. No serious drug-related adverse reactions were observed during the treatment process. In this study, four children with inflammatory myofibroblastic tumor received crizotinib for more than 2 months and achieved complete response, except for 2 cases with transient Q-T interval extension, with fewer side effects

overall. Therefore, crizotinib is currently a good choice for the surgical treatment of difficult and recurrent inflammatory myofibroblastic tumor in children.

关键字 Inflammatory Myofibroblastic Tumor(IMT) ; ALK gene; Crizotinib

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Current status and influencing factors of psychological resilience in adolescent leukemia survivors

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Objective： To explore the psychological resilience of adolescent leukemia survivors and analyze its influencing factors.
Methods： From October 2018 to August 2020, convenience sampling was used to select adolescent leukemia survivors in the routine follow-up group and follow-up group for children with leukemia who stopped taking medication in Beijing Children's Hospital affiliated to Capital Medical University as the research object. The General Information Questionnaire, Resilience Scale for Chinese Adolescents, and the General Self-Efficacy Scale were used to investigate adolescent leukemia survivors. A total of 110 questionnaires were issued, and 106 valid questionnaires were returned, with the effective response rate of 96.36%.
Results：Among 106 adolescent leukemia survivors, the total score of psychological resilience was （97.83±14.93）. The results of multiple linear regression analysis showed that disease risk, duration of drug withdrawal, and general self-efficacy were the influencing factors of psychological resilience in adolescent leukemia survivors, and the difference was statistically significant （P＜ 0.05）.
Conclusions：The psychological resilience level of adolescent leukemia survivors is at an upper-middle level. Medical and nursing staff, the family and friends of adolescent leukemia survivors should pay active attention to survivors whose disease risk is medium or high risk or whose duration of drug withdrawal is less than 5 years, and provide them with a lot of support and help. At the same time, pay attention to the general self-efficacy of survivors, provide targeted self-care guidance or substantive help for the survivors to return to school and society so as to improve their psychological resilience.

关键字 Leukemia; Adolescent; Survivors; Resilience, psychological; Influencing factors

分类：12. HaematologyOncology 血液与肿瘤
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CircKL inhibits the growth and metastasis of nephroblastoma by Sponging miR-182-5p and up-regulation of FBXW7

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Abstract **Background** Circular RNAs (circRNAs) are one type of non-coding RNA. They play an essential role in the regulation of various biological processes in malignant tumours. However, the potential molecular mechanisms and roles of circRNAs in nephroblastoma are still lacking. **Method** we analyzed our high-throughput microarray sequencing data to screen differentially expressed circRNAs in nephroblastoma. A novel circRNA (hsa_circ_0100312, named circKL) was identified as a frequently downregulated circRNA in both nephroblastoma cells and tissues. Both in vitro and in vivo experiments demonstrated that overexpression of circKL significantly inhibited the proliferation and metastasis of nephroblastoma. The molecular mechanism of circKL was studied by double luciferase report assays and RNA immunoprecipitation. **Results** The results revealed that circKL suppresses the growth and migration ability by sponging miR-182-5p and upregulating FBXW7 expression. **Conclusions** In conclusion, our study identified the biological role of the circKL-miR-182-FBXW7 axis in the growth and metastasis of nephroblastoma, which is curial for the monitoring and treatment of nephroblastoma.

关键字 Key words: circKL, circular RNAs, FBXW7, ceRNAs, nephroblastoma

分类：12. HaematologyOncology 血液与肿瘤
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Frustration of diagnosis and treatment for children's poorly differentiated chordoma: case report

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Background: Poorly differentiated chordoma (PDC) is a rare musculoskeletal tumor of the skull base and spine with a poor prognosis. The standard of diagnosis and treatment is not yet developed. Case presentation: The clinical data and follow-up outcomes of two children with chordoma were analyzed retrospectively. A restriction of neck movement of more than two- years' duration and complaints of neck pain of half-year duration occurred in two boys. Radiologic imaging revealed a contrast-enhancing soft tissue mass in the paraspinal and clivus regions with bone destruction. The final diagnosis of PDC was confirmed by microscopic examination and immunohistochemistry including brachyury, even though one of them had a misdiagnosis of INI1 (also known as SMARCB1)-deficient rhabdoid sarcoma. They both received chemotherapy and targeted therapy. One patient was in a control state again after relapse, while another died of disease progression. Conclusions: PDC is rarely seen in children and needs to be differentiated from diagnostic mimics. Multidisciplinary treatment especially including chemotherapy exhibits objective efficacy and may be a choice for this type of tumor.

关键字 Poorly differentiated chordoma, INI1, brachyury, chemotherapy, targeted therapy

分类：12. HaematologyOncology 血液与肿瘤
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Optimizing the method for differentiation of macrophages from human induced pluripotent stem cells

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Optimizing the method for differentiation of macrophages from human induced pluripotent stem cells

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1.Background

Macrophage is a very promising target for cancer therapy, yet it's very difficult to get enough functional macrophages for clinical cell therapy. Herein we establish a reliable method to produce functional macrophages through the differentiation of human induced pluripotent stem cells. In our protocol, we optimized the maturation time of macrophages and increased the yield of macrophages with no effect on the phagocytosis. It's worthy of being mentioned that hematopoietic differentiation originates from the outside of embryoid bodies (EBs) and matures inward gradually. M0 macrophages could be further polarized into M1 and M2 subtypes, and the phagocytosis was comparable to peripheral blood derived macrophages. Taken together, our results have important clinical implications for the development of macrophage in cell therapy and gene editing.

2.Method

2.1 HiPSCs Culture.
2.2 Differentiation of HiPSCs into Macrophages.
2.3 Flow Cytometry Analysis.
2.4. Wright-Giemsa Staining.
2.5. CD14+ Monocyte Isolation.
2.6. Differentiation of Macrophage Subtypes.
2.7. Fluorescent Beads Phagocytosis Assay.

2.8. Tumor Phagocytosis Assay.
2.9. Immunofluorescence.
2.10. Frozen Section and Immunofluorescence of EBs.
2.11. Cytokine Detection.
2.12. Statistical Analysis.

3. Results

3.1 The Quantity of Seeding Cells Affected the Process of HiPSCs Differentiated into Macrophages.
3.2. More Seeding Cells Promoted the Development of HPCs in EBs.
3.3. The hiPSCs Derived Macrophages Possess the Function of Phagocytosis.
3.4. Identification of the Different Polarization Subtypes from IPSDMs.

4.Conclusion

In the present study, the method of iPSCs derived macrophages were optimized. A new protocol was established which can promote the development of EBs and bring the maturation of macrophages forward. More importantly, with our protocol, the yield of macrophages was improved and the phagocytosis was not affected. In summary, our method can promote the clinical application process of iPSCs derived macrophages.

关键字 Induced pluripotent stem cells; Macrophages; Differentiation; Phagocytosis; Polarization

分类：12. HaematologyOncology 血液与肿瘤
964

Single-cell RNA-seq Reveals Characteristics of Tumor Heterogeneity and Cell Differentiation States in T-cell Lymphoblastic Lymphoma

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Objectives: T-cell lymphoblastic lymphoma (T-LBL) in children is a kind of disease with high aggressiveness, rapid disease progression, and poor prognosis, accounting for 80% of pediatric LBL cases. Different subtypes, risk stratification, and standardized treatment protocols have not been established for T-LBL patients, which affects prognosis and survival. We tried to dissect the origin of T-LBL, the direction of differentiation, and identify potential oncogenes for patient stratification and treatment outcome prediction by applying single-cell technology.
Methods: We performed single-cell RNA sequencing on tumor tissues from 3 patients, and bone marrow from a patient with T-LBL, as well as thymus tissues from healthy donors as normal controls. To investigate the ecosystem of T-LBL, we conducted cell clustering, gene expression program identification, gene differential expression analysis, RNA velocity analysis, and transcriptional regulatory networks analysis. We collected and retrospectively analyzed the clinical and pathological data from 42 patients with T-LBL at our hospital from 2010 to 2019 and establish the effect of potential oncogenes on overall survival.
Results: Based on transcriptional profiles in a single-cell resolution, we identified and characterized the malignant cells and immune subsets from 4 patients with T-LBL. There were 2 subgroups of malignant cells in T-LBL, related to the early stage and the late stage of T-lineage differentiation, respectively. The early-stage subgroup showed a block at the thymus seeding progenitor (TSP) and early T cell progenitor (ETP) stage, while the late-stage subgroup showed a block at the specified, committed, and rearranging stage. Transcriptional regulation analysis showed heterogeneity of the two subgroups, in which the early-stage subgroup related to hematopoietic stem cell key regulons, while the late-stage subgroup related to T-cell differentiation key regulons. Co-expression of MEF2C and CD34 identifies a subset of T-LBL patients with poor outcomes.
Conclusions: This work offers insight into the heterogeneity of T-cell lymphoblastic lymphoma, providing a better understanding of the transcription characteristics and differentiation heterogeneity of this tumor.

关键字 single-cell RNA-seq, T-cell lymphoblastic lymphoma, thymus

分类：12. HaematologyOncology 血液与肿瘤
1009

Childhood Localized Neuroblastoma has Favorable Outcome : A Single Center Report from CCCG-NB-2014 Study

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Background: Childhood neuroblastoma is a heterogenous group, in which localized and metastatic cases have definitely different outcomes. CCCG-NB-2014 Study led by Chinese Children’s Cancer Group refined risk-stratified treatment of neuroblastoma.
Method: 95 localized neuroblastoma from Xin Hua Hospital from 2014-2018 were enrolled. Most cases received surgery and chemotherapy based with cyclophosphamide and platinum.
Results：Risk factors for all kinds of events were analyzed by multivariate analysis. The median follow-up period was 48 months till July, 2020. 4-year event-free survival and overall survival for localized NB was 79.4%（95%CI：70.8-88.0%）and 88.2±3.6%（95%CI：84.6-91.8%）. Cases with N-myc gene amplification was the only risk factor after multivariate analysis with HR ratio 6.1（95%CI：1.4-10.8）.
Conclusion: Childhood Localized Neuroblastoma has Favorable Outcome. For cases with N-myc gene amplification, high dose chemotherapy under the rescue of autologous stem cell or immunotarget therapy were needed to further reduce the risk of treatment failure.

关键字 neuroblastoma, children, localized tumor, outcome, N-myc gene

分类：12. HaematologyOncology 血液与肿瘤
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Optimization of initial dose regimen for sirolimus in pediatric patients with lymphangioma

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Background: Sirolimus is an oral effective medication for pediatric patients with lymphangioma.
Methods: The present study aims to investigate the effects of underlying factors on clinical sirolimus concentrations by building up a population pharmacokinetic model, and to recommend initial dose regimen for sirolimus in pediatric patients with lymphangioma using Monte Carlo simulation.
Results: We found that the lower the body weight, the higher the clearance rate and sirolimus clearances were 0.31-0.17 L/h/kg in pediatric patients with lymphangioma, whose weights were 5-60 kg, respectively. The doses of sirolimus, 0.07, 0.06, 0.05 mg/kg/day were recommended for weights of 5-10, 10-24.5, and 24.5-60 kg in pediatric patients with lymphangioma, respectively.
Conclusions: This study was the first time to establish a population pharmacokinetic model of sirolimus, at the same time, the initial doses were recommended in pediatric patients with lymphangioma. Large-scale and prospective studies are needed in the future.

关键字 optimization, initial dose regimen, sirolimus, pediatric, lymphangioma

分类：12. HaematologyOncology 血液与肿瘤
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Genetic factors in Vincristine-induced peripheral neuropathy (VIPN): Can it be translated to improve the benefit and risk of cancer care in childhood acute lymphoblastic leukemia?

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Vincristine (VCR) is the first-line chemotherapeutic drug which is often coadministered with other chemotherapeutic drugs to treat childhood acute lymphoblastic leukemia (ALL). However, VCR possesses dose-dependent neurotoxicity, which is the main factor restricting its clinical application. VCR-induced peripheral neuropathy (VIPN) sometimes leads to dose reductions or omitted doses, which complicates its clinical outcomes and even affects patient's normal life after getting discharged from hospital. VIPN has characteristics including variable symptoms, unclear pathogenesis, and genetic differences between various individual patients, which results in its different pathological process. Therefore, it is not easy for clinicians to order this agent as an appropriate preventive or therapeutic measurements for cancer patients. With regard to the genetic basis of drug responses, pre-emptive pharmacogenomic testing and simultaneous blood levels monitoring could be helpful for translation of various findings into individualized therapies. Therefore, in this review, we discussed different genes and the potential associations between genetic variants that involved in the pharmacokinetics and/or pharmacodynamics of VCR and the incidence and severity of VIPN in cancer patients. Of note, genetic variants in CEP72 gene have great potential to be translated into clinical practice. Such genetic biomarker may help clinicians diagnose VIPN earlier so as to improve the effectiveness of treatment, reduce adverse reactions and improve the life quality of those cancer patients. Besides, genetic variants in other genes like CYP3A5, ABCB1, ABCC1, ABCC2, TTPA, ACTG1, CAPG, SYNE2, SLC5A7, COCH, MRPL47 have also been reported to be associated with the VIPN, but more evidence need to be accumulated in the future. In fact, a variety of complex factors jointly determine the VIPN. Such difficulties require combining genetics, environmental, and personal variables, as well as therapeutic drug monitoring in implementing precision medicine; and therefore facilitate better understanding the VIPN mechanisms so as to predict and improve the risk and benefit of VCR.

关键字 Vincristine; vincristine induced peripheral neuropathy; gene; pharmacogenomics; Polymorphism

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1343

Significance of anti-neutrophil antibody in chronic benign neutropenia in Chinese children

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Abstract Content Chronic benign neutropenia(CBN)is a primary autoimmune disorder characterizedby a self-limiting low neutrophil count below 1,500 cells per μL, lasting for at least 6 months.[1] It isdiagnosed by exclusion of other medical conditions that causes neutropenia. Itoften occurs at the age around few months old and resolved by few years old. Thetrue incidence of CBN is unknown as it is often an incidental finding during ablood count investigation. In the past decades, the immune nature of CBN hasbecome clearer. We know that it can be caused by granulocyte-specificantibodies. The detection rate of anti-neutrophilantibodies in patients with CBN is as high as 98-100% when several testingmethods are used.[1,2-3]. We plan to investigate the presence of anti-neutrophil antibody in chronic benign neutropenia (CBN) and its implication on severities of infection and disease recovery in Chinese children.

Methods This is a prospective cohort study conducted at a single center in the Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, Hong Kong. Chinese children who were under 18 years old of age and found to have neutropenia ≤ 1500 cells/uL lasting 6 months or more were recruited into the study between 2016 to 2018. Prior approval with the hospital Clinical Research Ethics and Institution Review Board was received. Information sheets are given and explained and informed consent was obtained. We excluded all patients with other causes of neutropenia for example: congenital neutropenia, cyclic neutropenia, neutropenia 'secondary' to allo-immunity, or other immune or systemic diseases, because the aetiologies, clinical manifestations, natural courses, and prognosis of these disease entities were different from those of CBN. Blood for anti-neutrophil antibody and genotyping was taken once at the time of recruitment and subsequently again when neutropenia recovered to ≥ 1500 cells/uL. These patients were followed up every 3 months with regular blood count monitoring for the duration they are neutropenic, anti-neutrophil antibody was repeated when the neutrophil count recovered. The cohort was followed up between the period of April 2016 until April 2021. A combination of two in house methods including Granulocyte Immunofluorescence Testing (GIFT), Granulocyte Agglutination Test (GAT) and one commercial kit LABScreenTM multipanel were used for the detection of anti-neutrophil antibodies. GIFT detects antibodies anchored on the patients neutrophils using fluorescent labelled anti human IgG and can be detected by flow cytometry or by fluorescence microscopy. Whilst GAT involves incubating patient's serum with neutrophils followed by microscopic evaluation for leucoagglutination.

A total of 100 participants were identified during the study period. One was excluded as he defaulted further blood taking, 6 were excluded as non-ethnic Chinese and 12 excluded for other causes of neutropenia found later on. Secondary causes for exclusion included: severe aplastic anaemia, severe congenital neutropenia, Schwachman- Diamond Syndrome, X-linked chronic granulomatous disease, haemophilia A,

acute lymphoblastic leukaemia. 81 participants with chronic benign neutropenia were qualified for the study. The age of onset, age of recovery, duration of neutropenia, gender, serial neutrophil counts, incidence of invasive infection, use of G-CSF were examined. Invasive infection was defined arbitrarily as infection requiring hospitalization plus either surgical intervention or intravenous therapy.
The Kaplan-Meier method was used to estimate median overall recovery time for the neutropenia patients. Two-sided 95% confidence intervals (CIs) for the median survival time were calculated by the Brookmeyer-Crowley method.

Results The baseline characteristics of the 81 participants were similar in the gender distribution (Female=37 (45.7%), the median age of onset was 3.7 months (1.1-48). The majority of patients presented with infection (n=39, 48.1%), predominantly viral infection (n= 29, 74%), whilst invasive infection made up 15%. The second most common presentation was incidental finding from blood taking in neonates with prolonged neonatal jaundice (n= 28, 33.3%). In the 81 participants with chronic benign neutropenia, anti-neutrophil antibodies were detected in 31% (n=25) of individuals. When comparing those with anti-neutrophil antibodies versus without, they were significantly older in age of onset (median, 6.7 versus 2.1 months, p=0.0029), more likely to have severe neutropenia on presentation (neutrophil count <500 cell/uL, p=0.0437), a lower median neutrophil count (p=0.0005) and more likely to have invasive infection (n= 6, 24% versus 4, 7.1% p=0.041). The majority of invasive infection occurred in the first year of diagnosis. Abscess was the most common presentation and methicillin-sensitive Staphylococcal aureus was the most common involved bacterial pathogen. The time for 50% recovery probability for this cohort of neutropenia patients was 2.34 years from onset (95% C.I. 1.98 to 2.71). Furthermore, anti-neutrophil antibody positive individuals were found to recover slower and later, the estimated median recovery time at 5 years follow up was 87.9% of anti-neutrophil antibody negative individuals recovered versus 69% of anti-neutrophil antibody positive individuals (p=0.035). Cox regression analysis found that the anti-neutrophil antibody status was independently associated with neutropenia recovery, whereas those with antibody-negative status had a 1.87 times higher chance of neutropenia recovery compared to antibody-positive individuals regardless of follow-up time and age of onset.

Conclusion It can be concluded that chronic benign neutropenia in Chinese children run a relatively benign course with 50% recovery at 2.34 years from onset of neutropenia. Anti-neutrophil antibody positivity was associated with more severe neutropenia, high likelihood of infection and slower and later recovery compared to those without.

Key words chronic benign neutropenia, anti neutrophil antibody
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1379

HAPLOIDENTICAL STEM CELL TRANSPLANTATION FOR PEDIATRIC PATIENTS WITH HIGH DONOR-SPECIFIC ANTIBODY (DSA) TITERS USING A DESENSITIZING CONDITIONING REGIMEN

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Abstract Content The application of haploidentical stem cell transplantation (haplo-SCT) greatly broadens the choice of donor pools for recipients of hematopoietic stem cell transplantation (HSCT). Recent evidence suggests that high donor-specific antibody (DSA) titer is one of the leading causes of graft failure that may contribute to higher transplant-related mortality and modality. Several approaches have been developed to reduce DSA. However, there is no available consensus or standard guidelines for the reduction of DSA for HSCT recipients due to limited evidence in published data. Our aims are to investigate the outcomes of pediatric haplo-SCT recipients with high DSA titers using a desensitizing conditioning chemotherapy regimen.

Methods Fourteen candidates of haplo-SCT aged 2 to 17 (median 8 years of age) were tested to have high DSA titers (HLA type I and/or HLA type II, MFI≥4000) between January 2020 and September 2020. Primary diseases included thalassemia major (13 in 14 patients) and severe aplastic anemia (1 in 14 patients). The conditioning protocol consisted of a cyclophosphamide-busulfan-based myeloablative regimen and was selectively given one or more approaches to reduce DSA titer, including high-dose intravenous immunoglobulin, rituximab, bortezomib, and plasma exchange. The GVHD prophylaxis consisted of post-transplant cyclophosphamide, mycophenolate mofetil, and tacrolimus.

Results Clinical data of 2 girls and 12 boys were analyzed. Haplo grafts were collected from the siblings (5/14), fathers (8/14), and mothers (1/14). The mean CD34+ cell dose was 12.52 × 106/kg. Neutrophil and platelet engraftment was achieved at a median of 20 days (range, 8-33 days) and 20 days (range, 8-40 days), respectively. No patients had graft failure nor had developed poor graft function. Only two patients developed grade I-II acute graft-versus-host disease (GVHD), and no chronic GVHD was observed. Viremia of cytomegalovirus (CMV) and Epstein-Barr virus was observed in three and two patients, respectively. However, none of these patients had CMV diseases or post-transplantation lymphoproliferative disorder. No other transplant-related complications were observed. All patients were alive without chronic complications at the time of last follow-up (median follow-up period 243 days, range 164 to 334 days).

Conclusion This preliminary data suggest that our approach to use a desensitizing conditioning regimen for pediatric recipients of haplo-SCT is safe and practical to limit graft failure and transplant-related complications and may contribute to a larger cohort study in the future.

Key words Haploidentical hematopoietic stem cell transplantation; Donor-specific antibody; Pediatrics

Reference NA

Category: 12. HaematologyOncology 血液与肿瘤
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Changes In Indonesian New Cancer Patients Visit To The Hospital Before And During The Coronavirus Disease 2019 (Covid-19) Pandemic

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Abstract Content Background: Cipto Mangunkusumo hospital (CMH) is the referral hospital including for. Pediatric Oncology patients. In accordance to the COVID-19 pandemic, non-urgent visit to the hospital were limited, and the patients themselves were also reluctant. However, problems arise mainly attributable to delayed treatment and difficulty in obtaining donors for blood transfusion. In this study we analyzed the difference in number of visits for new oncology patients and associated outcomes before and during the COVID-19 pandemic.

Methods Methods: This was a retrospective review study of pediatric oncology patients in CMH from January 2015 to December 2020. Data of all newly diagnosed oncology patients were collected including solid and non-solid malignancy. Each patient was counted once and changes in diagnosis when appropriate was not listed as a new patient. Total number of new cases were collected, and data from 2020 (pandemic) were compared with previous years (2015-2019). Outcomes were also collected and analyzed.

Results Results: This study included 1679 patients across 6 years of observation, with 219 patients (13%) from COVID-19 pandemic period and 1460 patients (87%) from baseline period. The majority of patients were non-solid tumors; 731 (44%) pre pandemic, and 117 (53%) post pandemic period, with ALL as the highest among all non-solid patients; 484 (29%) pre pandemic, and 87 (40%) post pandemic period. The number of cases fell from average of 292 to 219, with AML especially fell from average of 50 cases into 29 post pandemic. Outcomes was worse compared with previous years with higher mortality rate, readmission rate, and relapse, as well as lower number of remission. Associated factors include delayed treatment due to isolation treatment, COVID-19 co-infection, and worse clinical condition.

Conclusion Conclusions: There is a significant decline in newly diagnosed oncology patients, especially solid malignancy. The reluctancy and subsequent delayed treatment led to more advanced stages and worse clinical outcome on diagnosis. Despite the ongoing pandemic, extra attention still must be given to suspected malignancy cases, especially with the much improved COVID-19 screening and isolation which prevents delays in diagnosis and treatment.

Key words COVID-19; cancer; pediatric
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Category: 12. HaematologyOncology 血液与肿瘤
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Clinical management of Pancreatoblastoma in children

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Abstract Content Pancreatoblastoma (PB) is an extremely rare pancreatic tumor that commonly occurred in infant and young children [1,11]. It comprises less than 1% of pancreatic tumors. Clinical presentations of PB are diverse and nonspecific, which leads to diagnostic challenges. Biological aggressiveness and elevated levels of AFP show similarities to hepatoblastoma [34]. Imaging presentations brings differential challenges to neuroblastoma [35]. Diagnosis of PB relies on its distinctive histological features.

PB is commonly considered with an indolent course and achieve long-term survival with surgical resection alone [12,13], however, some studies show that the prognosis is poor when there is metastasis or incomplete resection [1]. The standardized management for risk stratification PB patients is rarely reported [6, 32]. Moreover, there is limited data about the standard clinical treatment of relapse and/or metastasis PB.

In our study, the clinical and imaging features, serum parameters, pathological diagnosis, and therapy are described in of pediatric PB, and relevant literature is reviewed, aiming to obtain better treatments for relapsed or metastatic patients.

Methods MATERIALS AND METHODS

Patients

In this study, 4 patients with PB hospitalized in our hospital between 2016 to 2020 were enrolled. Clinical data, including age at diagnosis, clinical presentation, site of disease, tumor size, serum α-fetoprotein (AFP) levels, treatment modalities and outcome, were reviewed. The assessments of tumor location, size, extent of the tumor, and distant metastasis were analyzed by ultrasonography (US), computed tomography (CT), or PET-CT (case 1). Treatment regimen of PLADO (cisplatin 80mg/m2 on day 1, and doxorubicin 30mg/m2 on day 2-3) and ICE (ifosfamide 1.5g/m2 on day 1-5, carboplatin 450 mg/m2 on day 1, etoposide 100 mg/m2 on day 1-3) were used. The literature search was conducted in the PubMed biomedical database, using the keywords as “pancreatoblastoma” and “pancreatoblastoma in children”. Additional papers derived from the references were also analyzed.

Histological and immunological analysis

All four patients were diagnosed according to the histopathology of tumors. The tissue was fixed with 10% buffered neutral formalin. Unstained 4-um sections were cut from each tissue’s specimens. Hematoxylin and eosin (HE), and immunohistochemistry staining was used for the histopathology analysis.Sections were stained immunohistochemically using cytokeratin, Ki-67, AE1/AE3, CK8, CK19, CK7, beta-catenin, Trypsin, AFP, VIM, synaptophysin (SYN), chromogranin A (CgA), CD56, VILLIN, CK5, CEA, and CDX2.

Results RESULT

1. Clinical features

Clinical features were shown in Table 1. There were three girls and one boy aged 3.6, 8.9, 4 and 5.5 years. Two patients presented with abdominal pain and two patients presented with palpable abdominal mass. Imaging findings indicated well-defined heterogeneous masses in the pancreas, with the tumor size of 7.6 cm, 5.2 cm, 10 cm, and 9.3 cm in maximum diameter, respectively. Invasion of splenic vein and

superior mesenteric artery, duodenum and lymph nodes were identified. Liver recurrence was shown in case 4. Two cases administrated combination therapy (preoperative chemotherapy, pancreaticoduodenectomy and postoperative chemotherapy), with a good outcome in the follow-up. Case 4 with invasion of splenic vein and superior mesenteric artery died of severe ascites and multiple metastases. Liver lobe resection was performed in case 3 and showed good outcome.

2. Pathological features

2.1. Morphology features

Neoplastic cells usually showed an organoid arrangement of acinar, solid, trabecular or ductal formations akin to acinar cell carcinomas (Fig. 2a). The solid component was made up of polygonal tumor cells with whorled or nests which was called “squamous corpuscles” (Fig. 2b). The nuclei were larger and more oval-shaped than those of the surrounding cells. Squamous corpuscles were detected in all the tumors.

2.2. Immunohistochemical staining

Immunohistochemical staining showed evidence of acinar, endocrine, and ductal differentiation, according to Trypsin, cytokeratin AE1/AE3, CK19, CK7, EMA, and VIM. Endocrine markers, such as SYN, CgA, CD56 were focal positive. Squamous corpuscles were positive for CK5 and EMA, but negative for CK7. Some of the immunohistochemical makers were shown in Fig. 2 c-h. Ki-67 ranged from 30-80%.

2. Case presentation

CASE 1

A 3-year and 6-month-old girl was hospitalized in our unit because of an abdominal mass for 2 weeks. No tumor family history was provided. Physical examination showed a palpable abdominal mass below the right costal margin line. AFP level reached to 2329.0 ng/ml (normal less than 20.0 ng/ml) and AFP variant was 278.48 ng/ml (normal 0-1 ng/ml). Raised serum LDH (508 U/L; normal range 106-211U/L) and NSE (69.8ng/ml; normal range 0-16.3 ng/ml) were presented. TORCH and hepatitis antibody were negative. US found a well-defined abdominal mass with heterogeneous echo in local hospital. CT revealed a 7.6×7.5 cm mass in the pancreatic head with heterogeneous components, which was characterized by flocculent calcification and clear rim. Rich vasculum was identified by CTA scan (Fig. 1a). As imaging of PET-CT (Fig. 1a) showed that the surrounding duodenum liver, gallbladder, and gastric wall were compressed by the tumor, tumor biopsy was performed though laparoscopic surgery according to multidisciplinary suggestions.

He was diagnosed as PB as pathological evidence. The patient was referred to oncologists and underwent four cycles of PLADO regimen were given, consisting of cisplatin 80mg/m2 on day 1, and doxorubicin 30mg/m2 on day 2-3. After the second cycle of chemotherapy, US revealed a 6.3×5.5 cm hypoechoic mass, with heterogeneous components, which was characterized by irregular, clear rim and punctate hyperechoic. After the fourth cycle of chemotherapy, CT showed that the tumoral size was reduced to 3.5×3.1cm. Flocculent calcification, as well as heterogeneous components were also identified. Serum AFP level reduced to 159.0 ng/ml, 10.4 ng/ml, 3.49 ng/ml, and 4.02 ng/ml, after the first, second, third, and fourth cycle, respectively. Similarly, AFP variant level was less than 0.6 ng/ml after third cycle.

Then, pancreaticoduodenectomy with Roux-en-Y end-toend cholangiojejunostomy was performed. After surgery, he was administrated PLADO pigment of chemotherapy

continuously for three cycles. Follow-up data showed a good outcome for 11 months. There was no residual tumor or recurrence on postoperative ultrasound and CT (Fig.1c). The level of serum AFP was always lower than 5 ng/ml and AFP variant was less than 0.6 ng/ml.

CASE 2

A 8-year and 9-month-old girl was admitted to local hospital with intermittent nausea for 2 months. A palpable abdominal mass was found by her parents for 1 month. No family members presented with tumors. Physical examination showed an abdominal mass without enlarged lymph nodes. US showed a heterogenous echoes in the middle of abdomen and para-aortic hypoecho nodules.

CT revealed a soft tissue shadow below the head of the pancreas with the size of 5.2×5.2 cm and surrounding lymphatic enlargement. Moreover, duodenum and superior mesenteric vein invasion were noted.

Laboratory tests showed elevated AFP level (323.00 ng/ml). Serum LDH (220 U/L; normal range 106-211U/L) and NSE (21.2 ng/ml; normal range 0-16.3 ng/ml) were slightly high. With these findings, biopsy of pancreatic head tumor was performed though laparoscopic surgery. The patient was diagnosed as PB according to the pathology results.

For further treatment, the patient came to our institution. Chemotherapy was given (cisplatin 80mg/m2 on day 1, doxorubicin 30mg/m2 on day 2-3). After first cycle of chemotherapy, tumor size was reduced to 4.1×3.5cm, and the serum AFP level came down to 20 ng/ml. After second cycle of chemotherapy, serum AFP level came down to 6.83 ng/ml and AFP variant was less than 0.6 ng/ml.

Then, pancreatoduodenectomy was performed. Four cycles of above chemotherapy were given after surgery. Follow-up data showed that there were no signs of recurrence for 9 months. AFP level was 0.91 ng/ml and AFP variant was less than 0.6 ng/ml.

CASE 3

A 5-year- and 5-month-old boy was suffered from abdominal pain for 1 month and was hospitalized in local hospital. An abdominal mass was detected by physical examination. Serum AFP was as high as 1064.31 ng/ml and a huge mass was found in the body and tail of the pancreas by US. Enhanced CT revealed a huge mass with a size of 10.7×7.1cm, and the duodenum was compressed by the tumor. Resection of pancreatic tumor was performed and PB was diagnosed based on morphological and immunohistochemical features. His family refused further postoperative chemotherapy because of socio-economic reasons.

After 10 months, he developed liver metastasis and was transferred to our unit. US showed liver mass with a size of 14.9×13.5cm. CT showed multiple intrahepatic nodules and enlarged portal /hilar lymph nodes with abundant blood vessels. Serum AFP increased to 121000.00 ng/ml. Four cycles of PLADO regimen were administrated. Serum AFP level reduced to 7069.00 ng/ml and 519.70 ng/ml, and the tumor size changed to 10.7×7.1cm and 6.8×5.3 cm by US after the first and second cycle, respectively. After the fourth cycle of chemotherapy, AFP value became to 36.85 ng/ml and tumor size was measured as 5.6×4.6 cm by CT examination. The patient underwent the segments 6 and 7 of the right liver lobe resection. AFP value decreased to 5.61 ng/ml in the first day after the surgery. Postoperative chemotherapy with cisplatin and doxorubicin was given for four cycles. Then, AFP level was 3.7 ng/ml. As CT scan showed multiple small abnormal signals in liver, further treatment was given according to ICE regimen as follow: ifosfamide (1.5g/m2

on day 1-5) , carboplatin (450 mg/m2 on day 1), etoposide (100 mg/m2 on day 1-3). Follow-up data showed that there were no signs of recurrence for 43 months.

CASE 4
A 4-year-old girl was suffered from abdominal pain for 3 months and was admitted to local hospital. Physical examination showed moderate jaundice of skin mucosa. CT showed a 9.3×8.8 cm heterogeneous mass with nodular calcification at right retroperitoneal. Adjacent organs of liver and gallbladder were compressed. Multiple tumor thrombi in splenic vein and superior mesenteric artery were detected. Laboratory examinations showed elevated serum AFP level (50.53 ng/ml). Ultrasound guided tumor biopsy was performed. According to the pathology results, she was diagnosed as PB.
Then, she was transferred to our unit and underwent chemotherapy of PLADO regimen. After one cycle, the patient's jaundice subsided, and AFP value came to 23.87ng/ml. After three cycles, AFP value became to 11.0 ng/ml and the tumor size was measured as 4.2×5.1 cm by CT examination. Tumor thrombi in splenic vein and superior mesenteric artery were still present.
Unfortunately, her family refused to subsequent treatment for socio-economic reasons. After 15 months, she died of progressive disease and multiple organ failure.

Conclusion In conclusion, PB is regarded as a curable tumor, and hence, a multidisciplinary diagnosis should be made early. “Squamoid nests” are considered as a defining component of histological diagnosis. Risk factors should be considered in therapeutic stratification of PB. Serum AFP levels may be useful for the diagnosis of pancreatoblastoma and follow up.

Key words pancreatoblastoma, child, treatment, chemotherapy, recurrence/relapse, metastasis
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分类：12. HaematologyOncology 血液与肿瘤
1441

Multi-Center Analysis of Recurrence in Children with Acute Lymphoblastic Leukemia Treated with SCCLG-ALL 2016 Protocol

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Background Although the outcome of childhood acute lymphoblastic leukemia （ALL） has been continuously improved in recent years, there are still some patients with recurrence, which significantly reduces the survival rate .This study is aimed to evaluate the recurrence and prognostic factors of acute lymphoblastic leukemiain children treated with South China Children’s leukemia Group ALL 2016 protocol（SCCLG-ALL 2016） by multicenter study and to guide early clinical intervention.

Methods One thousand seven hundred and thirty-nine newly diagnosed pediatric ALL treated with SCCLG-ALL 2016 protocol were included from eighteen hospitals of South China children’s leukemia Group from October 1, 2016 to July 31, 2020.Clinical features, laboratory results, recurrence and prognosis were retrospectively analyzed. Overall survival (OS) and event free survival (EFS) were analyzed by Kaplan Meier survival analysis, and the risk factors of relapse were analyzed by multivariate logistic regression model.

Results The median follow-up time was 20.67 (1.2-45.5) months. The 3-year overall survival rate (OS) of 1739 children was 93.7%±1.3%, and the 3-year event free survival rate (EFS) was 89.1%±1.8%. The recurrence rate was 3.6%（63/1739）, and the median recurrence time was 11.93 (2.1-41.8) months. The 3-year OS of recurrent children was 69.2%±14.1%.The proportions of very early recurrence, early recurrence and late recurrence were 71.4%, 26.9% and 1.6% respectively. The median survival time was 14.5 (2.07-36.0), 36.0 (19.2-45.6) and 41.8 months, respectively. Sixty-three cases of relapsed children were divided into bone marrow recurrence, extramedullary recurrence and bone marrow combined extramedullary recurrence according to the recurrence locations, accounting for 68.3%, 22.2% and 11.1% respectively. The median survival time of them was 20.2 (2.07-45.8), 17.6 (3.7-45.6) and 20.0 (3.1-33.3) months, respectively. Multivariate logistic regression analysis

showed that male gender (OR = 2.580, 95.0% CI 1.301-5.117, P < 0.01), age at first diagnosis < 1 year old and > 10 years old (OR = 2.333, 95.0% CI 1.268-4.292, P < 0.01), T-ALL (OR = 2.535, 95.0% CI 1.147-4.2426, P = 0.018), abnormal chromosome structure at first diagnosis (OR= 2.892, 95.0% CI 1.574-5.314, P < 0.01) was independent risk factors for the recurrence of ALL in children. **Conclusions** SCCLG-ALL 2016 protocol has significant therapeutic effect and low recurrence rate in the treatment of ALL in children. Very early recurrence and bone marrow recurrence have inferior outcome. Male gender, age at first diagnosis < 1 year or > 10 years, T-ALL and abnormal chromosome structure at first diagnosis are independent risk factors for the recurrence. Since the follow-up time of this study is short, it is necessary to extend the follow-up of time to reach a more accurate conclusions.

关键字 ALL , children , recurrence

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Analysis of gene mutations in predisposition gene based on transcriptome in children's acute lymphoblastic leukemia

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Abstract:
Objective: To analyze gene mutations in newly diagnosed childhood acute lymphoblastic leukemia (ALL) patients based on whole transcriptome sequencing.
Methods: Collected bone marrow specimens of 181 children with ALL who were first diagnosed in our hospital from September 2019 to June 2020; analyzed gene mutations through whole transcriptome sequencing; determine the pathogenicity of gene mutations through genetic database combined with the immune typing of the children; screened out and analyzed tumor susceptibility-related gene mutations.
Results: Among the 181 newly diagnosed ALL, 125 children (71%) detected 81 and 237 pathogenic or possibly pathogenic mutations, including 165 genetic mutations related to tumor genetic susceptibility; autosomal dominant tumors susceptibility gene mutations are the most common (104/165), of which RAS pathway mutations (82/104) are the main predominance; followed by tumor suppressor gene mutations (30/165), kinase mutations (28/165), autosomal recessive Sex tumor susceptibility gene mutation (3/165).
Conclusion: More than 50% of the children have detected pathogenic or possibly pathogenic gene mutations by using the whole transcriptome sequencing. The tumor genetic susceptibility-related gene mutations are the major concern.This result plays a key role to bulid the gene mutation spectrum of Chinese children with ALL, to further analyze its orgin (somatic or germline), to further observe the treatment response and prognosis of the children, finally to guide risk stratification, treatment selection and provide basis for target therapy.

关键字 acute lymphoblastic leukemia; whole transcriptome sequencing; gene mutation; tumor genetic susceptibility;

Category: 12. HaematologyOncology 血液与肿瘤
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Successful mesna intra catheter treatment in hemorrhagic cystitis post chemotherapy patients

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Abstract Content Cyclophosphamide and ifosfamide are an alkylating antineoplastic agents for chemotherapy with common side effect such as hemorrhagic cystitis. The incidence rates are 7% until 70%.[1] Cyclophosphamide is commonly used for the treatment of solid tumors and B cell malignancy.[2] Adverse effects of cyclophosphamide therapy such as bone marrow suppression, hemorrhagic cystitis, alopecia, pulmonary fibrosis, infertility and carcinogenesis.[3] Patient who received ifosfamide may also have a greater possibility to produce HC due to a high doses that administered. Acrolein are the urinary metabolite of cyclophosphamide and ifosfamide. Acrolein s believed to be responsible for the HC.[4] Because of the direct contact with the acrolein, the uroepithelial will get edema, ulceration, hemorrhage and necrosis.[5] Ifosfamide will be converted to the urotoxic metabolite and the accumulation of the metabolte in uroepithelial tissues will lead to HC. The treatments for HC had developed varied such as administration of large volume of i.v. fluid to promote diuresis, continuous 24 hours mesna infusion, urinary catheterization or combination any of the above, but there is still no gold standard of therapy.[6] The treatment of chemical hemorrhagic cystitis from chemotherapeutics focuses on prevention and then expectant management of hemorrhagic cystitis.

Methods All the data was collected from the electronic medical record. We report two cases of HC, the difficulty of the management and a brief review of the literature the management and the prevention.

Results Case Description:
Two pediatric patients who still suffered cyctitic hemmorhagic even after receiving infusions and intravenous 2-mercaptoethane sulfonate sodium (mesna) pre-treatment of cyclophosphamide and ifosfamide then treated successfully after intravenous and intravesical mesna. A seven years old boy with diagnose of forth grade osteosarcoma came to the hospital for the osteosarcoma chemotheraphy. Then he received mesna, cyclophosphamide, etoposide, carboplatin and leucogen. He received cyclophosphamide cumulative dose more than 3000 mg/m2/day for the first two days. On the fifth day of admission, after finishing the chemotherapy cycle he complained about dysuria and redness in his urine. Then he got mesna intravenous 1200 mg and mesna intracatheter 200 mg every twelve hours for his hematuria. He also got his complete blood examination and the result was anemia, neutropenia and thrombocytopenia. Then he got platelet transfusion for his trombocytopneia. He stil got mesna intracatheter treatment. The colour of his urine began to become clearer on the 14th day of the treatment. He also got his renal fumction test and ultrasonography of his renal. Both of the result of the test showed normal renal function. After 18 days of mesna intravenous and intracatheter treatment his urin become clear. The second case there's two years old boy with diagnose of rhabdomyosarcoma. He started his first chemoththeraphy that include ifosfamide, vincristine and dactinomycin in his regiment. He received ifosfamide cumulative dose 3000 mg/m2/day for the first two days. After finishing his first cycle of chemotheraphy he started to complained about dysuria, then we performed urine catheterization, the urine was mixed with blood. We perform red blood cell transfusion to the patient and mesna intracatheter 200 mg every twelve

hours for 7 days for the hemorrhagic cystitis. After 7 days of mesna intracatheter the urine become clear.

Conclusion Cyclophosphamide and ifosfamide (alkylating antineoplastic agents) induced hemorrhagic cystitis is one of a severe complication which can cause a significant morbidity. Various treatments have been reported, however there is still no standard of therapy for this complication. In this cases mesna can be used for the treatment if the hemorrhagic cystitis is already occurred but futher investigations should be demontrated.

Key words alkylating agent, hemorrhagic cystitis, 2-mercaptoethane sulfonate sodium, cyclophosphamide, ifosfamide

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分类：12. HaematologyOncology 血液与肿瘤
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Hyperleukocytosis in Childhood Acute Leukemia: management of a medical emergency

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Background
Hyperleukocytosis (HL) is defined as a white blood cell (WBC) count above 100,000/μL, caused by leukemic cell proliferation,and are common and fatal complications of childhood hematologic malignancieshas and has been independently associated with adverse outcomes.Here, we analyzed the clinical data of HL in acute leukemia(AL) children from the Chinese Children's Cancer Group (CCCG). This study was designed to assess the incidence of hyperleukocytosis, survival outcomes, and adverse features among pediatric acute leukemia patients with hyperleukocytosis.Te present fndings will help to get a better understanding of HL.

Methods
Between January 2015 and December 2019, 575 children with previously untreated AL（ALL＝472，AML＝103）were enrolled at West China Second University Hospital. All of them were initially stratified based on the Chinese Children's Cancer Group (CCCG) risk. The medical charts of these patients were retrospectively reviewed.
Results
Twelve (12%) of the 575 children with AL（69，AML＝14，ALL＝54）had initial leukocyte counts of ≥100x109/L, and 33（AML＝5，ALL＝28）patients had a leukocyte count of ≥200x109/L. Male gender, T-cell phenotype, and massive splenomegaly，various subsets of leukemia including myelomonocytic or monocytic/monoblastic morphology, microgranular variant of acute promyelocitic leukemia and cytogenetic abnormalities like 11q23 rearrangements,
inv(16), presence of the Philadelphia chromosome and molecular FLT3-ITD were positively associated with hyperleukocytosis. Common early complications during induction therapy included renal dysfunction, and central nervous system hemorrhage and DIC.
The estimated 3-year event free survival (EFS) and overall survival of AL children with hyperleukocytosis were 79.6% and 64.3%（ALL 43/54，AML 9/14）, respectively. However, patients with initial leukocyte counts ≥200x109/L had a lower EFS than those with initial leukocyte counts 100-200x109/L (60.2% vs. 100%; P=0.042).
Conclusion
The outcome of pediatric AL cases with an initial leukocyte count ＞200×109/L was very
poor, probably due to early toxicity-related death during induction therapy.

关键字 Pediatric acute leukemia，Hyperleucocytosis, leukapheresis, disseminated intravascular coagulation, tumor lysis syndrome

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LINC01296 promotes neuroblastoma tumorigenesis via the NCL-SOX11 regulatory complex

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Neuroblastoma (NB) is the most common extracranial solid tumor in childhood. Long noncoding RNA LINC01296 has been shown to predict the invasiveness and poor outcomes of patients with NB. In our study, we investigated the biological function and potential mechanism of LINC01296 regulating NB. We identified silencing LINC01296 inhibited NB proliferation in vivo and in vitro through CCK-8 assay, colony formation assay, EdU assay and xenograft tumor model, and promoted apoptosis through flow cytometry analysis and western blot analysis. The opposite results were observed when using the dCas9-SAM system activating LINC01296. Mechanistically, we revealed LINC01296 could directly bind to Nucleolin (NCL), forming a complex which activated SRY-box transcription factor 11 (SOX11) gene transcription and accelerated tumor progression by chromatin isolation by RNA purification (ChIRP), RNA-binding protein immunoprecipitation (RIP), and chromatin immunoprecipitation (ChIP) assays. In conclusion, our findings uncover a key role of LINC01296-NCL-SOX11 complex in NB tumorigenesis and may serve as a prognostic biomarker and effective therapeutic target for NB.

关键字 神经母细胞瘤 长链非编码 RNA 表观遗传学

分类：12. HaematologyOncology 血液与肿瘤
1705

The Expression, Clinical Significance and Mechanism of WASL in Acute Myeloid Leukemia

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Objective: To study the expression of WASL in acute myeloid leukemia(AML), to explore the relationship between its expression level and the prognosis of AML patients, to research the potential pathogenesis.Method: Firstly, the Cancer Genome Atlas database (TCGA) was searched and relevant clinical data of AML patients with WASL expression were downloaded. According to the median expression, the patients were divided into high expression group and low expression group. The correlation between the expression level and clinical indexes was analyzed; Then, bone marrow blood of patients who diagnosed as AML in our hospital from August 2020 to August 2021 was collected, these patients were divided into different groups according to the course of disease、 risk degree and immune classification; Non-tumor patients but with bone marrow puncture indications in our hospital at the same time served as the control group; The cDNA was extracted and detected by RT-PCR to analyze the correlation between WASL expression and prognosis. Finally, lentivirus plasmid was transfected into Jurkat cells to construct WASL overexpression leukemia cell line, proliferation level was detected by CCK-8, and the expression of apoptosis protein caspase-3 was detected by Western Blot (WB). Results: Database analysis showed that the overall survival rate of patients with low WASL expression was lower than that of patients with high WASL expression, the difference was statistically significant ; WASL expression level was an independent risk factor affecting the prognosis of AML patients. The results of patients aspects as follows: experiment group 60 cases, control group 20 cases. According to the immunotyping, the patients were divided into M0-M7 types, among them, M0 3 cases, M1 5 cases, M2 10 cases, M3 14 cases, M4 8 cases, M5 9 cases, M6 5 cases, M7 6 cases. According to the disease course, the patients were divided into newly diagnosed group, recurrence group and remission group, among them, newly diagnosed group 33 cases, remission group 10 cases, recurrence group 17 cases; According to the degree of risk, the patients were divided into high-risk group(HR), intermedium risk group(IR) and standard risk group(SR), among them, HR group 11cases, IR group 16 cases, SR group 33 cases. Compared with the control group, the expression of WASL in experiment group decreased significantly, and the difference was statistically significant; There was no difference in the expression of WASL in AML patients with different immunotyping compared with the control group; Compared with the control group, the expression of WASL in the newly diagnosed group decreased significantly, and the difference was statistically significant, while the expression of WASL in the recurrence group and remission group had no difference; Compared with the control group, the expression of WASL in HR group and IR group decreased significantly, and the difference was statistically significant; The proliferation rate of Jurkat cell line which stably overexpressing WASL was significantly lower than that of normal leukemia cell line; The expression of caspase-3 was detected by WB. The results showed that there was no difference in the expression of caspase-3 between the control group and Jurkat cell line which overexpressing WASL. Conclusions : WASL was low expressed in AML, the low expression of WASL in AML predicts poor prognosis; The expression level of WASL was correlated with risk degree and disease course, but have no relationship with immunotyping; WASL

participate in the pathogenesis of leukemia by affecting cell proliferation rather than apoptosis.

关键字 WASL; acute myeloid leukemia; prognosis; pathogenesis

Category: 12. HaematologyOncology 血液与肿瘤
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Vitamin D [25(OH)D] Levels in Children with Thalassemia Major

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Abstract Content Vitamin D is essential for optimal bone health, growth, and development in children. Vitamin D deficiencies are common worldwide and becomes an emerging concern, especially in thalassemia major. This study was to evaluate the vitamin D levels in thalassemia major children.
Methods A cross-sectional study design was conducted in children with thalassemia major aged 7-18 years at the Thalassemia Center at Cipto Mangunkusumo National Hospital. The classification is based on Global Consensus Recommendations on Prevention and Management of Nutritional Rickets whereas <30 nmol/L or <12 ng/mL are deficient, 30-50 nmol/L or 12-20 ng/mL are insufficient.
Results Vitamin D levels [25(OH)D] were measured using the enzyme-linked fluorescent assay (ELFA) method. We obtained 132 subjects (51,5% boys). Hypovitaminosis D occurred in 78,8% of the subject (32,6% deficiency; 46.2% insufficiency). The median level of vitamin D [(25(OH)D] was 18.1 (8-37) ng/mL. Hypocalcemia was found in 4.5% of subjects.
Conclusion Hypovitaminosis D is common in thalassemia, and they require regular vitamin D administration. Further research is needed to determine the optimal dose of vitamin D in children with thalassemia major.

Key words thalassemia, vitamin D, child
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分类：12. HaematologyOncology 血液与肿瘤
1790

Regulatory mechanism of damage chromosomes and mutate stem cells by endogenous alcohol produced from high-alcohol-producing Klebsiella pneumoniae

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Background
Haematopoietic stem cells could renew blood. The consumption of alcohol can cause DNA damage and impair the function of Haematopoietic stem cells (HSCs), which may lead to abnormal development, hereditary and devastating bone-marrow failure and cancer. Previously, we found that high-alcohol-producing *Klebsiella pneumoniae* (HiAlc *Kpn*) colonization of the intestine might cause NAFLD by continuously producing endogenous alcohol in the gut and proposed the etiology of non-alcoholic fatty liver disease (NAFLD)-endogenous alcoholic fatty liver disease. Meanwhile, we found that endogenous ethanol produced by HiAlc *Kpn* can cause severe haematopoietic disorder in mice. Whether the endogenous alcohol produced by HiAlc *Kpn* can cause the accumulation of DNA damage in HSCs, which contribute to the DNA interstrand cross-link and initiate the Fanconi anemia repair pathway (FA pathway)? Whether it makes the heritable chromosomal mutations and leads to a permanent genetic damage?
Method
In this study, we investigate the features and mutational landscape of DNA damage caused by endogenous alcohol and acetaldehyde in germ-free, $Aldh2^{-/-}$, $Fancd2^{-/-}$, and $Aldh2^{-/-}Fancd2^{-/-}$mice. Meanwhile, we combined transplantation of single hematopoietic stem cells with single cell sequencing technology to reveal the mechanism of chromosome repair mediated by microhomology in stem cell injury, and to determine the transmission pathway of p53 response regulating endogenous ethanol induced stem cell mutation.
Results
DNA damage caused by endogenous ethanol and acetaldehyde of HiAlc *Kpn* may be the cause of formation etiology of hematopoietic dysfunction of haematopoietic stem cells. And the p53 protein regulates the cellular response to DNA damage and induces damage recovery or apoptosis.
Conclusions
We attempt to determine the mutational landscape of individual HSCs, which caused by endogenous alcohol produced from high-alcohol-producing *Klebsiella pneumoniae*, and to provide new insight into the p53 response in mutagenized stem cells.

关键字 Metabolomics; Functional genome; high-alcohol-producing Klebsiella pneumoniae; Stem cell endogenous DNA damage; Fanconi anemia repair pathway.

Neurology

神经

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ASL 应用于儿童额叶癫痫术前定位

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Introduction: Epilepsy is one of the most common chronic neurological diseases, despite the great variety and prevalence of antiepileptic drug treatments, one-third of epilepsies remain drug-resistant. To our best knowledge, the patient reported in this case report is the first case of children with frontal lobe epilepsy achieving rapid and non-invasive surgical localization by ASL with EEG.
Objective: PET-CT is currently the main means of preoperative focal location for epilepsy, but it is expensive. ASL as a non-invasive fMRI examination, is expected to provide more examination options for preoperative focal location for epilepsy.
Methods: The clinical data of a child with drug-resistance epilepsy admitted to our hospital in 2020 were retrospectively analyzed, and relevant literatures were searched in the database for review.
Outcomes: A 4-year-old previously healthy girl was admitted to our hospital due to repeated seizures for 9 months, MRI was negative. Levetiracetam, clonazepam, oxcarbazepine, and lacosamide were successively administrated with poor outcome. Seizure control was not obtained from any of these treatments. The patient became seizure free after lesionectomy of the frontal lobe by arterial spin labeling (ASL) combined with electroencephalogram (EEG) rapid localization.
Conclusion: The positive outcome suggests that the combined use of ASL with EEG could be a beneficial option for presurgical evaluation of pediatric epilepsy.

关键字 arterial spin labeling, presurgical evaluation of epilepsy, frontal lobe epilepsy, drug-resistant epilepsy, focal cortical dysplasia.

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NPLR2 剪切突变所致 FFEVF

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NPRL2 (Nitrogen permease regulator-like 2) is a component of the GATOR1 complex, which is an inhibitor of the amino acid-sensing branch of the mTORC1 pathway. GATOR1 complex variations were reported to correlate with familial focal epilepsy with variable foci (FFEVF). However, FFEVF caused by NPRL2 variants has not been explored widely. Here, we describe a variant 339+2T>C in NPRL2 identified by Trio Whole-Exome sequencing (WES) in a family. This splicing variant that occurred at 5’ of Exon3 was confirmed by Minigene assays, which affected alternative splicing and lead to Exon 3 skipping in NPRL2. Our cases presented multiple seizure types (febrile seizure, infantile spasms, focal seizures, or focal to generalized tonic-clonic seizures). Electroencephalogram (EEG) showed frequent discharges in the left frontal and central region. A favorable prognosis was achieved by vitamin B6 and topiramate when he was seven-month-old. Our study expanded the phenotype and genotype spectrum of FFEVF, provide a solid diagnostic and therapy evidence for FFEVF.

关键字 NPRL2, neurodevelopmental disorder, familial focal epilepsy with variable foci, Whole-Exome sequencing

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SETD1A 突变所致神经发育障碍伴面容异常

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SETD1A(SET domain-containing Protein 1A) is a member of the COMPASS family of proteins, all of which have H3K4 methyltransferase activity and are closely related to neural development. Here, we describe a de novo variant c.2120_2121insA in SETD1A identified by Trio Whole-Exome sequencing (WES) in a child. The main manifestations of the children were mental motor development retardation, epilepsy, hypotonia, short stature, special facial features, hemangioma, enlargement of head circumference, toe deformity, white matter dysplasia, and ventricular dilation, etc. Compared to previous reports, in addition to the new gene mutation, our case showed phenotypic special face and toes deformities, on the left side of the facial features, trunk and limbs were relatively smaller on the right side. It enriches our understanding of SETD1A pathogenic neurodevelopmental disorders, expands the disease and genetic mutation data. In addition, we also found that the clinical phenotypes may be related to the types of mutations, and the truncating variants were more abundant in clinical phenotypes. Most of which are accompanied by mental and behavioral disorders, facial deformities, short stature, etc. It provides strong evidence for clinical diagnosis and genetic counseling.

关键字 SETD1A, Epilepsy, global development delay , Whole-Exome sequencing

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Case report of two anti-MOG antibody-related encephalitis after CNS infection and literature review

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Objective: Myelin oligodendrocyte glycoprotein (MOG) antibody disease is a rare autoimmune disorder with antibodies against the MOG predominantly involving the optic nerve and spinal cord leading to vision loss and paralysis. Here we presented two pedatrical cases with MOG antibody associated encephalitis, to improve the early diagnosis and treatment of this rare disease in pedatrical patients. Methods: Clinical data of 2 children with MOG antibody associated encephalitis admitted to our hospital in 2020 were analyzed, and published series were searched in PubMed, database until December 2020 for literature review. Results: A total of 2 children with MOG antibody associated encephalitis were collected. Case 1 was infected with EB-virus, and Case 2 was infected with Mycoplasma, both of whom had fever and headache as the main manifestations. Cranial MRI indicated multiple abnormal signals on cortical and cerebellum. Case 1 presented with progressed gait instability, accompanied by slower speech speed and reaction. EEG showed slowing background waves. The anti-MOG antibody IgG test was positive in both cases, and the initial titer was 1:10 and 1:100 respectively. The two children were given IVIG and steroid therapy, The therapeutic effect was good. Conclusion: MOG antibody associated encephalitis can occur secondary to a CNS infection, with no specific clinical characteristics, mostly subacute onset, some cases have a lrelative ong course. MOG-related antibody testing helps early diagnosis.

关键字 MOG antibody, MOG antibody related diseases, Acute disseminated encephalomyelitis, Infection induced ADEM

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West syndrome with KCNA2 gene mutation successfully treated by Topiramate: A case report

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Abstract Content West syndrome is a devastating disorder which is characterized by a triad of epileptic spasms, markedly abnormal electroencephalography (EEG), and developmental arrest or psychomotor delay. In addition to early diagnosis of the condition, it is important to find out its etiology. Among the various etiologies, genetic factor is common and critical, especially mutations of ion channel gene.

Methods A boy who had epileptic spasms from age of 4 months was diagnosed as West syndrome by clinical manifestation and EEG result in Shenzhen Children's Hospital in June 2019. Trios Whole-exome sequencing (WES) was performed and analyzed. The protein structural model precasting was analyzed by the Mutalyzer website and the SWISS-MODEL. Related literatures were searched on Online Mendelian Inheritance in Man (OMIM), Clinical Genome Resource (ClinVar), PubMed, Chinese National Knowledge Infrastructure (CNKI) and Wanfang databases with "KCNA2" "West syndrome" "Topiramate" as the key words up to December 2020. The clinical and genetic features of this syndrome on the related papers were discussed and summarized detailed. The action mechanism of topiramate (TPM) was also discussed. We tried to find out the relationship between the effect of TPM and the pathogenesis on KCNA2 mutation.

Results The proband is a 6- month- old boy who presented with epileptic spasms in the first 4 months after birth, hypsarrhythmia on interictal EEG, and developmental psychomotor delay. His clinical features are consistent with West syndrome. WES result shows the c.244C>T/p. Arg82Cys mutation of KCNA2 gene (NM_004974.3) in this patient, and Sanger sequencing identifies the mutation is de novo. Up to now, this novel mutation site of KCNA2 gene has not been reported. Besides, the novel mutation was likely pathogenic mutation according to the guidelines of the American College of Medical Genetics and Genomics (ACMG) in 2015. His seizures have been successfully controlled for 10 months by TPM after failure of Sodium valproate, large doses of vitamin B6 (VitB6), adrenocorticotropic hormone (ACTH). We speculate that the effect of TPM on this boy is partially due to the carbonic anhydrase inhibition.

Conclusion Mutations involving KCNA2 gene should be considered in patients with West syndrome. TPM treatment is probably effective on KCNA2-associated disorders.

Key words KCNA2 gene mutation, West syndrome, Topiramate

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分类：18. Neurology 神经
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A case of fatal encephalopathy caused by mitochondrial peroxidase division defect and literature review

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Objective: To explore the clinical features and disease-causing mutations of fatal encephalopathy caused by mitochondrial peroxidase division deficiency in order to improve the understanding of this rare disease. Methods: A child with fatal encephalopathy caused by DNM1L gene mutation in West China Second Hospital of Sichuan University was selected. The clinical manifestations, laboratory findings and disease-causing mutation were analyzed, related literatures were reviewed. Results: The main clinical symptoms of the patient were fever, headache and vomiting, followed by drug refractory epilepsy and progressive disturbance of consciousness. MRI showed deepening of sulcus, dilatation of bilateral ventricles, and multiple patch-like abnormal signals in paraventricular white matter, semioval center and subcortical white matter of bilateral frontal lobe. Gene detection showed a missense mutation in DNM1L (c.1207C>T, p.R403C, the variation was judged as pathogenic, PS1+PS2+PM2+PP3). After treated with gamma globulin, glucocorticoid, "mitochondrial cocktail therapy" and anti-epilepsy drugs, the condition of the patient was getting better, seizure attacks reduced and consciousness level improved. Conclusion: Fatal encephalopathy due to mitochondrial peroxidase division defect has an early onset developmental delay and drug-resistant epilepsy. DNM1L gene detection can help confirm the diagnosis, and early diagnosis and treatment may improve the prognosis.

关键字 Mitochondrial peroxidase division defect; Encephalopathy; DNM1L gene; Autosomal dominant inheritance

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Clinical Study of Somatosensory Music Physiotherapy Instrument on spastic cerebral palsy with child of muscle ton

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Clinical Study of Somatosensory Music Physiotherapy Instrument on spastic cerebral palsy with child of muscle ton

Abstract:
Objective: To observe the effect of somatosensory music physiotherapy instrument on relieving muscle tension in children with spastic cerebral palsy.
Method: 80 cases of children with spastic cerebral palsy were randomly divided into control group and observation group, 40 cases in each group. The observation group was treated with somatosensory music physiotherapy instrument, each treatment time was 20 minutes, 20 times was a course of treatment; The control group was treated with routine rehabilitation only. The joint range of motion, muscle tension and spasticity were measured before and after treatment. Results: the left and right muscle tension of the two groups both decreased after treatment than that before treatment, and the difference was statistically significant (P < 0.05). The left and right muscle tension of the observation group was better than that of the control group, the difference was statistically significant (P < 0.05); Before treatment, the two groups of children showed severe spasm, and the symptoms were relieved to moderate spasm after treatment, and the CSS score was also obviously lower, the difference was statistically significant (P < 0.05). The spastic symptom degree and CSS score of the observation group were lower than those of the control group, the difference was statistically significant (P < 0.05); The fast angle of left and right foot dorsiflexion and the slow angle of foot dorsiflexion of the children in observation group decreased obviously, the difference was statistically significant (P < 0.05); The left and right hip abduction angles increased obviously after treatment, the difference was statistically significant (P < 0.05)
Conclusion: The somatosensory music physiotherapy instrument can effectively relieve the muscle tension, spasm and muscle tone of patients with spastic cerebral palsy, and ultimately improve the patient's limb movement ability.
Keywords: spasm; somatosensory music physiotherapy instrument, muscle tone, muscle spasm

关键字 music physiotherapy instrument, muscle tone

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case report of UBA5 gene mutation caused developmental epileptic encephalopathy and literature review

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Objective　To summarize the clinical characteristics and gene mutation characteristics of a child with developmental epileptic encephalopathy (DEE) caused by UBA5 gene mutation, and to review the literature. Methods　A retrospective analysis of the clinical characteristics and genetic test results of a child with DEE who was admitted to Xuzhou Children's Hospital in March 2020. With "epilepsy encephalopathy", "developmental encephalopathy", "Epileptic encephalopathy", "Developmental encephalopathy" and "UBA5" as keywords, the database will be established through PubMed, CNKI, Wanfang and other domestic and foreign databases until June 2020 Relevant literature was searched, and confirmed cases of DEE caused by UBA5 gene mutations reported at home and abroad were summarized and analyzed. Results　Female, July 23 days, had seizures of seizures since April, but could not be controlled by ACTH and a variety of anti-epileptic drugs; the overall development of the child was backward, short stature, microcephaly, few facial expressions, and irritability. Unsteady head, unable to chase, unable to laugh, high muscle tone in the limbs; whole exome sequencing revealed that the child had a point mutation and CNV deletion in the UBA5 gene, and the point mutation was paternal c.722A>C(p.P241A), located in the 8th exon region, the CNV deletion is the maternally derived exon 5-11 region, which constitutes a compound heterozygous mutation. A total of 5 foreign documents (18 children) and 0 domestic documents were retrieved. A summary analysis of 18 confirmed foreign cases and this case showed that all 19 cases had intractable seizures in early infancy, most of which were in the form of seizures. Epilepsy seizures (63.2%, 12/19 cases), followed by myoclonus (31.6%, 6/19 cases). The birth history of all children was normal, and developmental disabilities of varying degrees appeared later, mainly microcephaly (94.7%, 18/19 cases), lack of follow-up vision (89.5%, 17/19 cases), and short stature (94.7%) , 18/19 cases), mental retardation (89.5%, 17/19 cases), dyskinesia (84.2%, 16/19 cases) and hypotonia (100%), most of them (68.4%, 13/19 Example) Has died. EEG may show normal or peak rhythm disorder, etc., and burst suppression occurred in 1 case. Head MR mainly included varying degrees of delayed myelination (47.4%, 9/19 cases), brain atrophy (52.6%, 10/19 cases), and dysplasia of the corpus callosum (26.3%, 5/19 cases).
Conclusion　Children with UBA5 gene mutations often have refractory seizures in early infancy, and the main types of seizures are seizures. In addition, they also present with severe psychomotor developmental retardation, microcephaly and dystonia, and the prognosis is extremely poor. , The fatality rate is high; head MR suggests varying degrees of myelin dysplasia, brain atrophy and corpus callosum dysplasia; for cases with the above clinical manifestations, genetic testing should be considered to confirm the diagnosis.

关键字 Developmental epileptic encephalopathy; gene mutation; UBA5 gene; children

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A case report of neonatal bacterial meningitis complicated by posterior fossa subdural pyosis and literature review

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Objective: To report a case of neonatal bacterial meningitis complicated by posterior fossa subdural pyosis and review the literature.
Methods: A 3-day-old neonate with gestational age of 37+6 weeks was admitted for jaundice with decreased milk intake for 1 day. In the hospital, test of the cerebrospinal fluid (CSF) showed a nuclear cell count of 1040×106/L, protein content of 2700mg/L, sugar value of less than 0.2mmol/L and chloride level of 119mmol/L. Pyocytes were found in the CSF. Culture of CSF and blood both indicated Escherichia coli. The diagnosis was neonatal sepsis and bacterial meningitis. CT of the head showed low-density area with crescent shape in the occipital extracerebral space. Head MRI indicated abnormal signals in this area with marginal enhancement. Posterior fossa subdural pyosis is considered with compression of adjacent cerebellar hemispheres. The size of subdural pyosis was about 2.1cm×1.1cm on the left side and 1.7cm×0.9cm on the right side.
Results: After 5 weeks treatment of meropenem combined with ceftazidime, the symptoms were relieved. Reexamination of CSF showed a nuclear cell count of 4×106/L. Reexamination of head MRI showed decreased size of subdural pyosis and thickening of the occipital meninges. The lesion on the left side was about 1.4cm×0.6cm, and the lesion on the right side disappeared. However, there was dilatation of the lateral ventricles and the third ventricle indicating hydrocephalus. Omaya capsule implantation and decompression of intracranial pressure were performed in the neurosurgery department. Then the child was discharged with follow-up.
Conclusion: Posterior fossa subdural pyosis is a rare complication of bacterial meningitis, which is a critical disease of the central nervous system. Due to lack of specific manifestation, it could be misdiagnosed easily if the early head imaging fails to show prominent signs. CT or MRI of the head demonstrate a posterior fossa subdural fluid lesion with marginal enhancement. It is necessary to take active antibiotic therapy with enough course. Subdural pyosis may gradually subside after the use of antibiotics but requires close observation. If antibiotic treatment is not effective, surgery may be necessary. The posterior fossa subdural pyosis caused by bacterial meningitis may be combined with hydrocephalus, and CSF shunt surgery should be performed if necessary.

关键字 subdural pyosis； bacterial meningitis; posterior fossa; neonate

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Clinical features, treatment and outcomes of 33 Northwest Chinese children with Anti-N-methyl- D - aspartate receptor encephalitis

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Objectives: We analyzed the clinical features and outcomes of children with anti-N-methyl- D －aspartate receptor (anti-NMDAR) encephalitis in Northwest China.

Methods: We retrospectively recruited 33 pediatric patients with anti-NMDAR encephalitis in Northwest China from December 2013 to April 2020. Demographics, clinical features, treatment, and outcome were reviewed.

Results: 33 patients with anti-NMDAR encephalitis were enrolled (age from 9 months to 13 years old; median age: 6.8 years ; 20 females) in this study. The initial symptoms included seizure in 14 patients (42.4%), psychiatric symptom in 13 (39.4%), speech dysfunction in 4 (12.1%), and paralysis in 2 (6.1%). During course of the disease, 31 patients (93.9%) presented with psychiatric symptoms, 29 (87.9%) with speech dysfunction, 25 (75.8%) with movement disorders, 24 (72.7%) with sleep disorders, followed by seizures, consciousness disturbance, autonomic nervous dysfunction, paralysis, and hypoventilation. 12 patients (36.4%) had abnormal cerebrospinal fluid (CSF) findings, 10 patients (30.3%) exhibited abnormal brain magnetic resonance imaging (MRI) results, and 29 patinets (87.9%) showed abnormal Electroencephalography (EEG) findings. None had tumor. All patients received first-line immunotherapy, 8 patients both received first-line and second-line immunotherapy. 30 of the 33 patients achieved good outcomes (score on the modified Rankin Scale [mRS] of 0－2), while the other 3 had poor outcomes (mRS score of 3－6).

Discussion Read tips: Abnormal cranial MRI findings, intensive care unit (ICU) stay and autonomic instability were predictors of poor response to first-line immunotherapy. Patients with higher CSF anti-NMDAR body titer were more likely to develop sleep disorder, consciousness disturbance and more severe disease states.

关键字 anti-NMDAR encephalitis, clinical feature, treatment, outcome, children

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Association oO Blood Type with the Prognosis of Acute Necrotizing Encephalopathy in Childhood: A Single-center Cohort Study

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Background: Acute necrotizing encephalopathy (ANE) of childhood is a rare but critical disease with global distribution. Few studies focused on investigating the relationship between O blood type and the prognosis of ANE.
Methods: We retrospectively analyzed the data of ANE patients admitted to Beijing Children’s Hospital from March 2012 to February 2019. The baseline data, clinical characteristics, examination, treatment and prognosis of O blood group were compared with that of non-O blood group. Cox regression was used to observe the independent prognostic factors in ANE.
Results: Thirty-one ANE patients were recruited, 8 patients (25.8%) in O blood group and 23 patients (74.2%) in non-O blood group. There was no significant difference between two groups in demographic characteristics, clinical features, examinations and treatments ($p > 0.05$). Twenty-eight days after discharge, the overall survival rate of O blood group was significantly higher than that of non-O blood group ($\chi 2 = 5.630$, $p = 0.018$). One year after discharge, the survival quality of O blood group was higher compared with non-O blood group ($p = 0.006$). After adjusting for confounding factors, cox regression analysis showed that O blood type might be a protective factor in ANE [hazard ratio (HR) (95% CI) = 0.283 (0.081-0.988), p= 0.048].
Conclusions: O blood type may be a protective factor for ANE patients.

关键字 Acute necrotizing encephalopathy; O blood type; Prognosis; Children

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MTHFR is not a possible risk factor for febrile seizures

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Abstract
aims To clarify whether rare monoallelic variations of mthfr contribute to febrile seizures as a mild phenotype.
Method A total of 850 febrile seizure patients with febrile seizures were recruited from 2018.12-2019.7.31 national wide. mthfr variations in these 850 febrile seizures patients were reanalyzed.
Result Two patients with biallelic mthfr variations and another 39 monoallelic mthfr carriers were found carrying 19 rare variations (4 unreported). Among those with positive family history for febrile seizures, only 50% were found inherited the rare variations from the affected parents. The frequency of mthfr variations (2.0%) among febrile seizures' population was even lower than that in 1000 unrelated health control (4.4%). There was more c.677(rs1801133) CT types among febrile seizures while more TT type among health controls.
Interpretations The thermolability of MTHFR didn't make it a possible contributor for febrile seizures.

关键字 febrile seizures, MTHFR, homocysteine, thermolability

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Sirolimus in Tuberous Sclerosis Complex prior to epilepsy: evidence from a registery-based real world study

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Abstract

Background： To evaluate if sirolimus in tuberous sclerosis complex patients prior to epilepsy relieve the later burden of new-onset seizures.

Methods： A real world matched case-control trial was nested in another cohort study. For early sirolimus group, children (<1year old) who were diagnosed as tuberous sclerosis complex and had no seizures but taking sirolimus for other symptoms were eligible. For the late sirolimus group, age and genotype were used as the first-place stratifying criteria for 1:4 frequency matching, other symptoms of baseline condition were also assessed between the two group. None preventative drug should be introduced before seizures or before 2 years old in those without seizures in late sirolimus group. Subjects were enrolled from 2015 to 2018 and followed up until June 2020. The main outcome was the change of characteristic of seizures and the final condition of seizures.

Results： A total of 42 patients were included in the early sirolimus group, and 168 were matched in the late sirolimus group. Early sirolimus significantly reduced seizure-onset especially for infants < 6month old. The mean onset-age was significantly delayed by sirolimus (11.34±7.93month vs. 6.94±6.03month, P < 0.001). The subtypes of seizures benefit most was infantile spasm (5/42, 11.90% vs 73/168, 43.45%, P < 0.001) which might be eliminated or alleviated. Adding sirolimus prior seizures performed better than adding after seizures in reducing refractory seizures (10/42, 23.81% vs 70/147, 47.62%, P = 0.004). Seizures related to tuberous sclerosis complex might be none fever-related.

Conclusions: Early sirolimus intervention in tuberous sclerosis complex can prevent some seizures, especially infantile spasm. Early sirolimus modified the disease, delayed seizure-onset and relieved the severity.

关键字 tuberous sclerosis complex, sirolimus, infantile spasm, partial seizure, febrile seizure

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Mitophagy in Nervous system diseases

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Mitophagy in Nervous system diseases

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Background
In all kinds of cells in human body, there are different basic levels of organelle autophagy to maintain cell metabolism and homeostasis, such as mitochondrial autophagy, endoplasmic reticulum autophagy, ribosome autophagy and so on. Among them, mitochondria, as an energy plant in eukaryotes, are particularly important for tissues with strong energy demand. At present, mitochondrial autophagy has been studied in various organs and tissues of human body, such as brain, heart, kidney and tumor. Our next discussion is about the mechanism of autophagy in the nervous system. Autophagy is important for quality control of nervous system cells, Because many of the central nervous system cells are postmitotic.

Method
Importantly, the mechanisms of mitophagy are involved in chronic diseases of the nervous system, such as neurodegenerative diseases. However, carfilzomib, a drug for multiple myeloma therapy that inhibits proteases, can restore the mitophagy of neurons and prevent acute or chronic ischemic brain injury by reversing Bnip3L degradation, suggesting that mitophagy may not play a role only in chronic diseases of the nervous system.

Results
At present, studies on mitochondrial autophagy in chronic diseases of the nervous system are mainly based on neurodegenerative diseases. The pathological feature is the disharmony between the accumulation of aggregation proteins and damaged organelles in the involved neurons and organelles, protein clearance mechanisms such as mitochondrial autophagy, leading to the aggregation of damaged organelles and polyubiquitinated proteins in neuronal cytoplasm and nucleus.
Compared with chronic diseases of the nervous system, there have been relatively few studies on mitochondrial autophagy in acute diseases of the nervous system. These include studies on stroke, ischemic and hypoxic brain injury, epilepsy, and traumatic brain injury. The pathological mechanisms are complex and different, but have aspects in common, such as acute injury that activates mitophagy, and an imbalance between autophagy and autophagy flux causes abnormal autophagy mechanisms. There is still no consensus on whether mitophagy is beneficial or harmful.

Conclusions
At present, there are many studies on mitochondrial autophagy in nervous system, mainly focusing on the molecular level of its pathogenesis. In some aspects, these studies provide new ideas for targeted therapy of nervous system diseases in the

future. However, it is still controversial to choose and utilize the most appropriate targeted therapy. In addition, the current studies on the mechanism of mitochondrial autophagy mainly tend to focus on the long-term chronic diseases of the nervous system. What is the specific mechanism of action in the short-term acute diseases of the nervous system? There is still a lack of a large number of rigorous studies to confirm that this is what we need to do at present and in the future.

关键字 Mitophagy signaling pathway，Neural system diseases

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Clinical study of CASPR2 antibody encephalitis in children

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Objective To investigate the clinical features, laboratory tests, electroencephalogram (EEG) manifestations, treatment and prognosis of CASPR2 antibody encephalitis in children. Methods One preschool child diagnosed with CASPR2 antibody encephalitis and suffering from the illusion vision, fear, fidgeting with abnormal movement and other mental and behavioral abnormalities, hypersomnia and hyperhidrosis was admitted in the Department of Neurology of Xuzhou Children's Hospital on February 27th, 2020. The clinical features, laboratory tests, EEG manifestations, treatment and prognosis of the patient were retrospectively analyzed. The relevant literatures were searched, and the clinical characteristics and therapeutic effects of the cases were reviewed. Results The clinical features of this case were abnormal mental behaviors, normal cranial imaging and abnormal video EEG: slow waves, multifocal sharp slow wave and spike wave in the central and posterior head, Serum anti-Caspr2 antibody 1:32. After 3 weeks of treatment with gamma globulin and steroids, phantom vision and fear disappeared, Abnormal movements gradually decreased, sleep and sweating were significantly improved. He could communicate with others and read numbers below 10 fluently, but he can simply add and subtract. The titer of serum anti-Caspr2 antibody decreased. Six months later, there were only involuntary movements such as shaking hands and clapping hands, the EEG was normal, the antibodies in blood and cerebrospinal fluid were negative, and the brain MRI was normal. The symptoms disappeared one month after oral administration of tiapride. In the review of relevant domestic literature, there were no similar cases of children reported; in the foreign literatures reported there were 3 cases of CASPR2 antibody positive: 2 cases were diagnosed as CASPR2 encephalitis, methylprednisolone and gamma globulin was the first choice for treatment, and the curative effect was significant, which was consistent with the treatment of this case. One case was diagnosed as Kleine-Levin syndrome, and the symptoms were relieved after oral administration of oxcarbazepine.
Conclusion: Children with CASPR2 encephalitis have a variety of clinical symptoms, including cognitive dysfunction, seizures, autonomic nervous disorders, good response to gamma globulin and methylprednisolone, and good short-term prognosis after treatment.

关键字 Children; immune Encephalitis; CASPR2; hallucinations; Mental and Behavioral abnormalities

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anti-myelin oligodendrocyte glycoprotein antibody-associated disease with total spinal cord injury: A case report

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Background：anti-myelin oligodendrocyte glycoprotein antibody-associated disease with total spinal cord injury: A case report
Method：Anti-myelin oligodendrocyte glycoprotein (MOG) antibody associated disorders frequently manifest as optic neuritis, transverse myelitis, and acute disseminated encephalomyelitis. While their clinical phenotypes overlap with relapsing inflammatory Central nervous system (CNS) conditions such as multiple sclerosis and neuromyelitis optica spectrum disorder, MOG-related syndromes frequently occur in a younger age group. In children, longitudinally extensive transverse myelitis (LETM) is less specific for anti-aquaporin-4 associated neuromyelitis optica spectrum disorder, and has also been reported in pediatric multiple sclerosis, idiopathic transverse myelitis, and acute flaccid myelitis.
Results：We summarize one patient with positive MOG antibodies and diffuse abnormal signals in the spinal cord-myelitis.
Conclusions：Anti-MOG diseases can cause ADEM with total spinal cord injury and increased awareness of the disease.

关键字 MOG;ADEM

分类：18. Neurology 神经
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The relationship between the spasticity-related pain and the quality of life about the cerebral palsy in China

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Purpose：Children and adolescents with cerebral palsy suffered from spastic pain that effected their quality of life. The purpose of this study was to examine the relationship between the spasticity-related pain and the quality of life about the children with cerebral palsy with spasticity-related pain in China.

Methods：This was a prospective, observational, one-arm multicentre study. 137 cerebral palsy children with SRP and their parents/caregivers were recruited from three sites in China. The children and their parents/caregivers completed the Questionnaire on Pain Caused by Spasticity and PedsQL TM 4 scale.

Results：137 children with their parents/caregivers were eligible for participation in the study, and all completed the relevant investigation. According to the result of the children-report PedsQL, the total scale scores in the V2/V3 about the different age groups (5-7years old ,8-12 years old, 13-16 years old) had no statistic significance((P > 0.05). After 3 weeks, the change compared to first time survey result was not significant (p>0.05). The total scores and each domain of PedsQL in the CP with SRP was lower than the normal group (P<0.05). On the whole, the associations between the child and parent proxy-report QPS total scores and each domain scores of PedsQL were moderate to high. The PedsQL total scores relationship to the QPS item score was moderate.

Conclusion; The quality of life in the CP patients with SRP was worse than normal people and it was a steady long-term stage. The correlation between the spasticity-related pain and the quality of life was moderate to high and negative and the result from the parent proxy-report was more evident.

关键字 cerebral palsy children; spasticity-related pain; quality of life

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Mosaicism and phenotype in 264 genetic epilepsy families detected by Amplicon-based Deep Sequencing

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Background: To investigate the occurrence of mosaicism and severity of phenotype in epilepsy families by amplicon-based deep sequencing (ADS).
Method: Two hundred and sixty-four probands with pathogenic variants identified in 44 epilepsy genes were enrolled. The frequency of mosaicism was detected in probands and their parents using ADS. All probands fulfilled one of the following criteria: (1) probands carried pathogenic variants which were identified as "de novo" in blood by Sanger sequencing; (2) suspected mosaicism in probands or parents was presented by Sanger sequencing or NGS; (3) siblings of the probands had the same phenotype and carried the same gene variation, but their parents had no epilepsy phenotype and did not detected the variants by Sanger sequencing; (4) one of the parents had the history of seizures, proband had been detected the pathogenic variants of epilepsy gene, but none of potentially pathogenic variant was detected by Sanger sequencing of the parents. Probands fulfilled one of the following criteria should be excluded: (1) pathogenic variants were copy number variations; (2) genetic pattern was autosomal recessive.
Results: A total of 264 pathogenic variations were collected, which were identified in the blood samples of probands with epilepsy. Pathogenic variations occurred in 44 genes. The average sequencing depth covering pathogenic variants was 88,909x. KCNQ2, SCN2A, STXBP1, SCN8A, SCN1A and CDKL5 were the most frequently detected mosaic genes. Of 264 families, 31 probands or parents had mosaicism (20 probands, 5 paternal and 6 maternal) in 17 genes. The frequency of observed mosaicism was 11.74% (31/264). Mosaicisms of genes including COL4A1, CSNK2B, FGF13, and SLC1A2 had never been reported previously. Mosaicism in genes including CACNA1A, COL4A1, CSNK2B, FGF13, GABRB3, KCNB1, KCNQ2, KCNT1, SCN2A, SCN8A, and STXBP1 were identified from twenty probands with the mutant allelic fractions (MAFs) of 12.95%-38.00% in autosomal dominant genes. Five paternal mosaicisms were identified in genes including KCNA2, SCN1A, SCN2A, SCN8A and STXBP1 with the MAFs of 6.30%-20.99%. Six maternal mosaic individuals were identified in genes including KCNT1, SCN1A, SCN2A, SLC1A2, STXBP1, and WDR45 with the MAFs of 2.07%-21.90%. The seizure onset age of 20 mosaic probands was ranged from 1 day after birth to 7 years. One patient was diagnosed as Ohtahara syndrome (OS), three patients were West Syndrome (WS), and seven patients suffered developmental and epileptic encephalopathy (DEE). All 20 probands showed developmental delay (DD). Ten probands presented abnormal brain magnetic resonance imaging. Eleven probands with parental mosaicism experienced seizures. The onset ages of 11 probands ranged from 3 days after birth to 2 years. One patient (patient 21 with KCNA2 variant) was diagnosed as epileptic encephalopathy with continuous spike and waves during slow-wave sleep (CSWS), one patient (patient 23 with SCN2A variant) as OS, one patient (patient 25 with STXBP1 variant) as OS developed to WS, one patient (patient 26 with KCNT1 variant) as epilepsy of infancy with migrating focal seizures (EIMFS), one patient (patient 28 with SCN2A variant) as WS, and two patients (patient 24 with SCN8A variant and patient 29 with SLC1A2 variant) was DEE. All eleven patients manifested DD. MRI was abnormal in five patients. Only four mosaic parents had milder seizure history. The affected sibling had the same phenotype

consistent with the proband in two families, who inherited the variant of SLC1A2 or STXBP1 from their unaffected mosaic mothers, the MAFs were 21.37% and 20.87%, respectively.
Conclusions: Mosaic phenomenon is not rare in families with epilepsy. Phenotypes of mosaic parents were milder or normal. Mosaicism detection is helpful to identify the mutation origin and it provides a theoretical basis for prenatal diagnosis of family reproduction. ADS is a reliable and effective way of mosaicism detection for clinical application.

关键字 epilepsy; mosaicism; next-generation sequencing; amplicon-based deep sequencing

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Genetic spectrum identified by exome sequencing in a Chinese paediatric cerebral palsy cohort

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Abstract
Background Due to the high genetic heterogeneity of cerebral palsy (CP), further studies are needed to further reveal its genetic underpinnings. This study aims to explore the genetic spectrum of CP in a Chinese paediatric cohort.
Methods Patients with CP were recruited from the Children’s Hospital of Fudan University between June 2015 and December 2019. Clinical data were collected, and exome sequencing was performed in all patients.
Results A total of 217 CP patients were enrolled, and genetic variants were identified in 79 subjects (36.4%, 79/217): 66 patients (83.5%, 66/79) with single-nucleotide variants (SNVs), 12 (15.2%, 12/79) patients with copy number variants (CNVs) and one patient (1.3%, 1/79) with both an SNV and a CNV. The genetic diagnosis rates were significantly higher in patients without clinical risk factors than in patients with clinical risk factors (c2=19.994, P=0.000). Variants in genes related to neurologic disorders were the most commonly detected variants, affecting 41 patients (61.2%, 41/67). Among the patients with SNVs detected, the top 12 genes were found to cover 61.2% (41/67) of cases, and 38.8% of patients with SNVs had medically actionable genetic findings.
Conclusions The overall genetic diagnostic rate in this study was 36.4%, and patients without any clinical risk factors were more likely to have genetic risk factors. The top 12 genes detected in this study, as well as genes related to neurologic disorders or medically actionable disorders, should be noted in the analysis of genetic testing results in CP patients.

关键字 cerebral palsy; exome sequencing

分类：18. Neurology 神经
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Research progress of nanomaterial-based blood-brain-barrier (BBB) crossing strategies in brain tumors

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【ABSTRACT】 **OBJECTIVE** This paper reviews the research progress of nanomaterial-based blood-brain barrier (BBB) crossing strategies in brain tumors, in order to explore the feasibility research direction in the future. **METHODS** This paper reviews the limitation of the BBB on the delivery of peripheral substances to the central nervous system(CNS) under physiological and brain tumor conditions, as well as the current research methods of BBB drug delivery system model, and puts forward a variety of intracerebral drug delivery strategies based on nanomaterials. **RESULTS** The existence of the BBB greatly limits the drug treatment of brain tumors, and the permeability of most antineoplastic drugs to the brain parenchyma is quite limited. The delivery of drugs crossing into the CNS through the BBB is a major challenge in the development of neurotherapy. Due to the advantages of high drug loading, controllable drug release, good passive or active targeting, good stability, biodegradability, biocompatibility and low toxicity, nanomaterials with BBB crossing have been widely developed for targeted therapy of brain tumors. **CONCLUSION** BBB plays a very important role in maintaining the normal physiological function and pathological state of the central nervous system. With the rapid development of nanotechnology, brain tumor therapeutic drugs based on nanomaterials show great potential in the BBB crossing strategies. Although many nanomaterials have been approved by FDA or undergoing clinical trials, the clinical application of nanomaterial-based BBB crossing strategies is still limited.
KEY WORDS: Brain tumor; Blood-brain barrier; Nanomaterials; Crossing delivery; Targeting

关键字 Brain tumor; Blood-brain barrier; Nanomaterials; Crossing delivery; Targeting

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Anti-ANNA2-associated neurodevelopmental delays in pediatric patients

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Abstract:
Objective: To describe anti-Ri autoantibody-positive (Type II anti-neuronal nuclear antibody; ANNA-2-positive) autoimmune encephalitis occurred with intellectual and development disabilities.
Method:We presented the clinical manifestations, etiological evaluation, and intellectual assessment of ANNA-2-positive children and the clinical improvement after empirical immunotherapy.
Result:A 2-year-old girl with hyperactivity, agitation, and hand tremors and a 6-month-old boy who had dystonia were both diagnosed with intellectual and development disability. Both children tested positive for ANNA-2 and the serological inflammatory markers. Considerring possible Ri antibody associated autoimmune encephalitis, empirical immunotherapy was done for both patients, intellectual disability of them improved to some extent.
Conclusions: Although ANNA-2 has been mostly reported in adults with paraneoplastic syndrome, we report two ANNA-2-positive pediatric cases diagnosed as possible autoimmune encephalitis due to viral infections. These cases suggested that disruption of the immune system due to viral infection may lead to ANNA-2 positive status and contribute to intellectual and development disability in pediatric cases.
Keywords: intellectual disabilities, Ri antibody, autoimmune encephalitis

关键字 : intellectual disabilities, Ri antibody, autoimmune encephalitis

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Pediatric anti-NMDAR encephalitis: association between clinical features, cerebrospinal fluid characteristics, and brain MRI findings

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Background: Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is the most common autoimmune neurological disorder in children. However, studies focusing on the association between clinical symptoms, cerebrospinal fluid (CSF) results, and brain magnetic resonance imaging (MRI) findings, especially the association between CSF immunoglobulins and brain MRI findings are still limited. Thus, this study aimed to analyze the associations mentioned above and unveil the partial underlying immune mechanism involved in the process of abnormal brain MRI of the disease.
Methods: We conducted a study of pediatric patients diagnosed with anti-NMDAR encephalitis who were admitted to Xinhua Hospital Affiliated Shanghai Jiaotong University School of Medicine, between 2016 and 2020. Clinical features were collected. Serum and CSF measurements, and brain MRI were performed after admission. The associations between clinical symptoms, CSF results, and brain MRI findings were analyzed.
Results: Twenty-seven pediatric patients diagnosed with anti- NMDAR encephalitis were enrolled in the study. The age of the patients was 73.15 ± 38.47 months, and nineteen (70.4%) patients were female. Fifteen (55.6%) patients had CSF leukocytosis (> 5/mm3), and total protein concentration was 248.40 (204.00-441.30) mg/L. CSF IgG, IgA, and IgM levels were 25.60 (12.50- 43.20), 2.18 (1.34-3.37) and 0.94 (0.63-3.44) mg/L, respectively. Intrathecal IgG, IgA, and IgM synthesis was observed in 30.4%, 39.1%, and 60.9% of the patients. IgG and IgM indexes were 0.62 (0.53-0.72) and 0.30 (0.10-0.44). Eight (29.6%) patients exhibited abnormal brain MRI findings, with T2 or fluid-attenuated inversion recovery (FLAIR) hyperintensity. The ratio of fever in patients with abnormal brain MRI findings was significantly higher than that in the normal brain MRI group (p = 0.026); The IgM level in the CSF and IgG index were significantly higher in patients with abnormal brain MRI findings than that in the normal brain MRI group (p = 0.016 and p = 0.015, respectively).
Conclusion: Pediatric anti-NMDAR encephalitis patients with abnormal brain MRI findings had a significantly higher ratio of premonitory infectious symptoms, and higher CSF IgM level and IgG index were significantly associated with abnormal brain MRI findings. These new findings, might reveal a partial mechanism of brain MRI abnormalities in patients with anti-NMDAR encephalitis.

关键字 Pediatric anti-NMDAR encephalitis; clinical features; CSF results; brain MRI findings;

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A small molecule targeting p75NTR reduces neuroinflammation in experimental Streptococcus pneumoniae meningitis

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Objectives: Streptococcus pneumoniae meningitis (PM) is a destructive bacterial infection of the central nervous system (CNS), and its unfavorable prognosis usually results from an intense inflammatory response. Compelling evidence provided by previous studies suggests that p75 neurotrophin receptor (p75NTR) signaling influences cell survival, apoptosis, and proliferation in brain-injured conditions. This study aims to determine the role of p75NTR and the therapeutic potential of LM11A-31, a small-molecule p75NTR modulator, in reducing PM-induced brain injury.
Methods: First, the activation of p75NTR in the PM model was detected by western blot. During acute PM, a small-molecule p75NTR modulator LM11A-31 or vehicle was intranasally administered for 3 days prior to S.pneumoniae exposure. The changes of body weight, survival rate and Loeffler neurological score were assessed during acute meningitis. At 24 hours after infection, histopathology and microglia/astrocytes activation of brain tissues were evaluated. Additionally,
hippocampal apoptosis was assessed using terminal deoxynucleotidyl transferase dUTP-nick-end labeling (TUNEL). Inflammatory factors levels were determined using real-time polymerase chain reaction (RT-PCR).
Results: Our study found that the expression of p75NTR was significantly increased in the cortex and hippocampus following PM. Modulation of p75NTR through pretreatment of PM model with LM11A-31 significantly alleviated S.pneumoniae-induced clinical severity, histopathological injury and the activation of astrocytes and microglia. LM11A-31 pretreatment also significantly ameliorated hippocampal apoptosis. Moreover, we found that LM11A-31 decreased the expression of inflammatory factors (IL-1β, TNF-α, IL-6 and iNOS) in the cortex and hippocampus.
Conclusions: Our findings suggest that the p75NTR plays an important role in the pathogenesis of PM. LM11A-31 targeting p75NTR has benefit effects on PM by alleviating neuroinflammation. Thus, p75NTR may be a potential therapeutic target to improve the outcome of PM.

关键字 p75NTR , Streptococcus pneumoniae meningitis, neuroinflammation

分类：18. Neurology 神经
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BDNF 通过活化 TrkB-Akt-STAT3 信号通路抑制小胶质细胞介导的炎症反应

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The development of neurodegenerative disease and infectious neuropathology is always accompanied by neuroinflammation, which is characterized by microglial activation. Accumulating evidence has revealed that brain-derived neurotrophic factor (BDNF) has protective effects on diverse central nervous system (CNS) diseases. However, the potential anti-neuroinflammatory activity and mechanism of BDNF in microglia-mediated inflammation remain largely unclear. In this study, we sought to investigate the role of BDNF in microglia-mediated inflammation and the underlying mechanism in in vitro and in vivo models of lipopolysaccharide (LPS)-induced neuroinflammation. Here, we showed that BDNF dose dependently suppressed the expression of pro-inflammatory factors, and increased the expression of M2 markers in microglia. Mechanistically, BDNF controlled the expression of inflammation mediators and microglial polarization through tropomyosin-receptor kinase B (TrkB) phosphorylation and subsequent Akt-STAT3 pathway activation. In vivo pretreatment with BDNF significantly reduced LPS-induced expression of pro-inflammatory cytokines, pathological severity, microglial activation and neuronal injury and increased anti-inflammatory cytokine expression in the brains. Together, our data indicate that BDNF could modulate microglial M1/M2 polarization and suppress the microglia-mediated neuroinflammatory responses via activation of TrkB-Akt-STAT3 signaling, thereby providing a potential therapeutic strategy for neuroinflammatory pathologies.

关键字 BDNF，microglia，neuroinflammation

分类：18. Neurology 神经
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Anti-viral methods can improve prognosis of infantile spasm combined with Cytomegalovirus infection

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Backgroud: As the most important epileptic encephalopathy, Infantile spasm(IS) can lead to refractory seizures and serious mental retardation. Reasons of IS is various, So find the exact cause and do targeted treatment is important. Cytomegalovirus infection among people is common and IS patients is also often combined with CMV infection. So We investigated this kind of infants and try to find some interaction of CMV and IS and try to find new methods to improve prognosis.
Method: Retrospectivly investigation were carried out to find the IS infants combined with CMV infection. Patients' clinicial information were collected first, including age, gender, blood test, EEG data, cranial MRI, seizure frequecy and sometimes CSF. After anti-epilepsy and anti-virus therapeutic methods carried out, Seizures, Intelligence development and EEG results were recollected to assess treatment efficiency.
Result:19 ISs combimed with CMV infection were investigatied in this study, with 2 CMV Ig-M antibodys positive in blood and the others CMV-DNA positive in urea. The M/F gender ration is 12:7, and average age of onset is 5.8months. As for etiology, 4 babies got birth asphyxia, 1 baby is cranial hemorrage, 1 baby is congenital CMV infection and 3 deno gene were found among them. After anti-viral and anti-epilepsy treatment, 58%(11/19)infants got completely controlled, although 27% relapsed(3/11), 4 of them seizures were controlled effectively, so total response rate is 79%(15/19); then 4 didn't have any effect, although we try our best. EEG reviews shows hypsarrhythmia were disappeared in 12 babies; and 6 babies got great improvement of intellectual development.
Conclusion: IS is an intractable epileptic encephalopathy and etiology is various, and often combined with CMV infection. Combined anti-epilepsy and anti-viral treatment can greatly improve the prognosis of infant spasm, what ever seizures control, EEG or intellectual improvement. CMV infection is an potential reason of IS and should be emphasized in our clinical practice.

关键字 infantile spasm，Cytomegalovirus，infection

分类：18. Neurology 神经
1121

nde1 Deficiency in Zebrafish Induces Brain Inflammatory Responses and Autism-like Behavior

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Background: Clinical studies have shown that deletions in the Nde1 are closely related to autism and mental retardation, etc. Studies showed Nde1 plays an important role in the process of neural development and maintenance of normal neuro system functions. However, the cellular molecular mechanisms beneath the neuropsychiatric disorders are not fully elucidated yet.
Methods: In this study, we investigated the expression pattern of nde1 during zebrafish development, and generated nde1 homologous deficiency zebrafish (nde1-/-) through CRISPR-Cas9. The effects of nde1 knockout were investigated by morphological observation, neurological apoptotic analysis and behavioral analysis. The molecular mechanism of nde1deficiency pathogenesis was then explored by neurotransmitter-targeted metabolome and transcriptome analysis combined with qRT-PCR quantitative analysis of differentially expressed genes (DEGs).
Results: Here we noticed that nde1 expression is at highest around 24hpf-30hpf in early development and after 2mpf. nde1-/- exhibit increased neurological apoptotic responses at 30hpf, increased luminal spaces between the brain structures and reduced valvula cerebelli in adult brain tissue. At both 30hpf and 3mpf, pidd1 and bbc3 which promote the apoptosis are increased, bcl2a and bcl2l which inhibit the apoptosis are decreased. Behavioral analysis revealed that nde1-/-displayed increased locomotor activity, increased frequency of repetitive behaviors and impaired social behaviors and kin recognition. Molecular mechanism exploration revealed that nde1 knockout resulted in significantly increased levels of serotonin (5-HT) and normetanephrine (NMN) in adult brain. DEGs were enriched in infection and immune-related pathways, with increased expression of inflammatory factors in the brain and enhanced inflammatory responses.
Conclusions: nde1 homologous deficiency results in neurological apoptosis, abnormal brain structure and autism-like behaviors. Molecular fundamentals of which includes inflammatory responses in the zebrafish brain and significantly increased levels of 5-HT and NMN.

关键字 Nde1, pro-inflammation cytokines, autism, repetitive behavior, 5-HT

分类：18. Neurology 神经
1130

Genetics and clinical phenotypes of epilepsy associated with 1p36 deletion syndrome

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Genetics and clinical phenotypes of epilepsy associated with 1p36 deletion syndrome

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【Abstract】 **Objective** To summarize the genetics and clinical phenotypes of epilepsy in children with 1p36 deletion syndrome. **Methods** All the patients with 1p36 deletion syndrome were retrospectively collected at the Pediatric Department of Peking University First Hospital from March 2017 to July 2021, the features of clinical manifestations, electroencephalogram and neuroimaging were analyzed. **Results** Twelve patients with 1p36 deletion syndrome were included. All 12 patients had de novo copy number variation (CNV) with a deletion size between 1.38 and 8.1 Mb. The main genes in the region were *MMP23B*、*GABRD*、*SKI* and *PRDM16*. Age at seizure onset ranged from 17 days to 5 months, and the median age was 2 months and 7 days. Multiple seizure types were observed, included epileptic spasm in 11 patients, focal seizures in 5 patients, tonic seizures in 2 patients, myoclonic seizures in 1 patient. Developmental delay was presented in all 12 patients. All 12 patients had craniofacial anomaly, including a flat nasal bridge, straight eyebrows, deeply set eyes, low-set ears, cleft lip and protruding ears. Eight patients had abnormalities in other systems, including congenital heart defects in 5 cases, hearing abnormalities in 4 cases, hemangioma in 3 cases, renal calculi in 1 case, congenital cataract in 1 case, micropenis in 1 case and a single transverse palmar crease on both hands in 1 case. Brain magnetic resonance imaging (MRI) showed enlargement of subarachnoid spaces in the frontal and temporal region in 3 patients, deep sulcus in 2 patients, enlargement of bilateral lateral ventricle in 4 patients, white matter hypoplasia in 3 patients, agenesis of corpus callosum in 1 patient. In 12 patients, nine patients were further diagnosed with Infantile spasms. The age at last follow-up were ranged from 13 months to 8 years and 5 months, two patients were seizure-free for 19 months to 2 years, one patient died of unknown cause, and 9 patients still had seizures. **Conclusions** The main pathogenic genes in the deletion region of 1p36 deletion syndrome include *MMP23B, GABRD, SKI* and *PRDM16*. The seizure onset age of 1p36 deletion syndrome related epilepsy was in infancy. The main seizure types include epileptic spasm and focal seizure, and most patients are fit the diagnosis of Infantile spasms. Seizures are difficult to control in most patients. All patients had developmental delay and craniofacial anomaly, some patients have abnormalities in other systems.

关键字 1p36 deletion syndrome ,Epilepsy, Infantile spasms, craniofacial anomaly, prognosis

分类：18. Neurology 神经
1144

The clinical and imaging characteristics of pediatric pineal region tumors

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Objective: We evaluated the characteristics of chinical data and imaging findings of pediatric pineal region tumors to improve the accuracy of preoperative diagnosis.
Methods: 20 cases of pediatric pineal region tumors confirmed by pathology were analyzed retrospectively.
Results: 20 children including 15 males and 5 females with pineal region tumors were identified: 12 with germ cell tumors (including 5 germinomas, 4 teretomas and 3 mixed germ cell tumors), 5 with pineoblastomas, 1 with pineal parenchymal tumor of intermediate differentiation, 1 with anaplastic astrocytoma and 1 with ganglioglioma. 12 patients of germ cell tumor were including 11 males (92%) and 1 female with a mean age of 9.1+3.6 years. 8 patients had a high serum level of AFP (>5 ng/ml). The imaging appearances were variable and the mean ADC value was 1138+407*10-6 mm2/s. Germinomas were homogenous on CT and MRI with intense enhancement and the mean ADC value was 841+115*10-6 mm2/s. Teratomas and mixed germ cell tumors were heterogeneous with intratumoral calcification and cysts. The mean ADC value in teratomas and mixed germ cell tumors were 1376+361*10-6 mm2/s and 1316+459*10-6 mm2/s respectively. 5 patients of pineoblastoma were including 3 males and 2 females with a mean age of 5.3+5.2 years. The conventional CT and MRI findings were similar to those of germ cell tumors. The mean ADC value in pineoblastomas (646+81*10-6 mm2/s) was lower than that of germ cell tumors ($p<0.01$).
Conclusion: Germ cell tumors are the most common tumors of the pediatric pineal region tumors. Most patients are males. The imaging appearances are variable. It's important for radiologists to combine the imaging findings with tumor markers. The incidence of pineoblastomas is also high. They usually involve younger children. ADC values can aid in differentiation of pineoblastomas from germ cell tumors in children.

关键字 Pediatric pineal region tumors, MRI, DWI

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1184

Neuroimaging characteristics and genetic correlations in pediatric mitochondrial disorders: a cohort study from China

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Background and Objectives Mitochondrial disorders present with high clinical, genetic and neuroimaging variability. The spectrum of neuroimaging phenotype expanded fast based on the expanding of molecular etiologies. **Methods** In this study, we prospectively recruited a cohort of pediatric mitochondrial disorder patients, who were diagnosed with definite genetic results and available neuroimaging results in the Neurology Department of Children's Hospital of Fudan University, from January 2011 to October 2020. The clinical presentation, neuroimaging data and genetic results were collected and reviewed. **Results** Our study enrolled 77 patients (42 boys and 35 girls) with primary mitochondrial disorder, including 54 patients who harboured mtDNA mutations (70.1%) and 23 patients with nDNA mutations (29.9%). The positive rate of brain MRI findings (85.7%) was higher than CT (66.7%). The most common MRI findings were deep nuclei lesion (71.2%), brain atrophy (63.6%), cortical and subcortical white matter lesion (30.3%), deep white matter (30.3%), and diffused cerebral atrophy (10.6%). T1WI revealed hypo-intensity signal in 83.2% MDs, T2WI showed hyperintensity signal in 92.6% MDs and 70.7% of lesion demonstrated restricted diffusion. Lesion in deep white matter, symmetrical deep nuclei lesion, and specific corpus callosum involvement was more common in nDNA-mutated patients (p=0.0365, p=0.0158 and p=0.0286). Lesion in multi deep nuclei was observed almost all groups of biochemistry deficiency but more common in patients with dysfunction of OXPHOS subunits; cortical and subcortical white matter lesion was more common in mtDNA-mutated patients with dysfunction of mtDNA maintenance, expression and translation; and lesion in deep white matter was more common in patients with dysfunction of metabolism of cofactors. Deep nuclei lesion was observed most frequently in patients with mutations in *MT-ATP6*, *MT-ND6*, and *NDUFAF5* genes. Among the group of patients who had cortical/subcortical white matter lesion in MRI, mutations in *MT-TL1* gene, mtDNA large-scale deletion, and *NDUFAF5* were most common. Stroke-like and deep nuclei lesion were often concurrent in patients with m.3243A>G mutation. **Conclusions** Neuroimaging features overlap in variable mitochondrial disorders. There is some correlation between neuroimage phenotype and genotype as well as biological defects.

关键字 mitochondrial disorder; pediatric; computed tomography; magnetic resonance imaging; genotype; neuroimaging

分类：18. Neurology 神经
1209

PACS gene family related neurological diseases: limited genotypes and diverse phenotypes

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Background: PACS (phosphofurin acidic cluster sorting protein) gene family has been demonstrated to be related to intracellular vesicular trafficking. The PACS gene family in humans includes two genes, PACS1 and PACS2, which are highly homologous. The phenotypes caused by PACS gene family neurological diseases mainly included epilepsy, intellectual disability/developmental delay (ID/DD), and malformations such as facial abnormalities. Method: Seven cases with PACS gene family related neurological diseases were diagnosed by trio-whole exome sequencing (trio-WES). For patient with suspected causative CNV found by WES, we performed whole genome sequencing (WGS) to identify the extent of CNV and analyze the pathogenicity. We collected all previously reported cases with PACS gene family related neurological diseases on PubMed, and combined all cases to analyze the features of PACS gene family related neurological diseases. Results: We reported six patients with PACS2 related neurological diseases, one of whom carried a novel de novo heterozygous deletion of chr14:105821380-106107443 (286 Kb) and the other five all carried a reported pathogenic variant (c. 625G > A [p.Glu209Lys]). In addition, we reported one patient with PACS1 related neurological diseases, carrying a reported pathogenic variant (c. 607C > G [p.Arg203Trp]). Up to now, including cases newly diagnosed in our study, there were 78 cases of PACS gene family related neurological diseases reported. These included 25 cases of PACS2 related neurological diseases and 53 cases of PACS1 related neurological diseases. All cases of PACS2 related neurological diseases had seizures, and 96% (24/25) of them had seizures as the first symptom. 60% of cases of PACS1 related neurological diseases had seizures. Many types of ASMs (anti-seizure medications) have been reported to be effective, and the most commonly used and effective ASMs were sodium valproate (39.3%, 11/28), oxcarbazepine/carbamazepine (32.1%, 9/28), and levetiracetam (17.9%, 5/28). Almost all patients (77/78) with PACS family genes related neurological diseases had ID/DD. The severity varies widely. Most (76/78, 97.4%) of patients had facial abnormalities. 68% (17/25) of patients with PACS2 related neurological diseases had abnormal brain MRI. Patient carrying heterozygous deletion of chr14:105821380-106107443 (286Kb) had a later age of onset of epilepsy and ID/DD and more severe and refractory seizures were seen. The most common pathogenic missense variant of PACS2 was p. Glu209Lys (92% of patients), located in the auto-regulatory region of the MR (middle region) of the protein. The most common pathogenic missense variant of PACS2 was p. Arg203Trp (98% of patients), located in the FBR (furin-binding region) of the protein. Conclusions: We reported patients with PACS gene family related neurological diseases in Chinese population and expanded the genotypes. We combined all cases to analyze and found epilepsy, ID/DD and structural abnormalities were the main manifestations of PACS gene family related neurological diseases. Seizures were relatively easy to control by ASMs. The clinical phenotypes caused by heterozygous missense variants were similar. The phenotype of patient carrying heterozygous deletion of chr14:105821380-106107443 (286Kb) was more severe than that of patients carrying missense variants. The main functional regions of PACS1 were similar as PACS2, and their pathogenic variant sites were both quite limited. However, the variant sites of PACS1 and PACS2 were in different regions. This suggests that MR of PACS family proteins might

regulate the function of whole protein through intramolecular interactions with FBR. We summarized the characteristics of phenotype and genotype of PACS gene family related neurological diseases. These results may provide important clues for further functional studies of PACS family proteins and the pathogenic mechanism of related neurological diseases.

关键字 PACS1, PACS2, epilepsy, ntellectual disability/developmental delay

分类：18. Neurology 神经
1238

Multi-model fusion classification method based on EEG signal

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Background
Epilepsy is a common neurological disease, which usually causes supersynchronous discharge. In clinical practice, epilepsy needs to be diagnosed with brain electrical signal detection. The patient is usually tested for epilepsy disease by means of drug induction. In this process, the acquisition time of EEG signals is usually as long as tens of hours. Doctors need to determine epileptic seizures from dozens of hours of data. EEG interpretation is time-consuming and laborious, which is a heavy burden on doctors. For this reason, designing an automatic detection method for epilepsy EEG signals has important clinical significance.
Methodology
Due to the powerful end-to-end learning capabilities of deep learning, deep learning methods have been widely used in the task of classifying epilepsy EEG signals. The traditional classification method of epilepsy EEG signals mainly uses a single model to extract the temporal features contained in the EEG signal. However, epilepsy usually has super-synchronous discharge of the whole brain, and the cooperative discharge relationship between different channels is also a very important feature. For this reason, we use different models to extract the waveform features of the EEG signal and the cooperative features of the multi-channel EEG signal. To comprehensively and accurately analyze epileptic EEG signals. In addition, the model that takes into account the features of a single EEG signal channel in the traditional epilepsy classification task only needs to perform feature extraction and model training. However, in the multi-model integration method of fusing the cooperative features of multi-channel EEG signals, it is necessary to consider the huge differences between the features extracted by different models. For this reason, we designs a feature fusion module to effectively create different models. The extracted features are fused.
Results
In order to effectively verify the method proposed in this paper. We conduct experiments on the classic CHB-MIT dataset. The dataset is collected at the Children’s Hospital Boston. The data contains a total of 23 epilepsy EEG data for subjects (one subject collected it twice). We compared the performance of different methods on the dataset and found that different models were used Extracting different features of multi-channel EEG signals has better classification performance.
Conclusions
We design a multi-feature fusion deep learning epilepsy EEG signal classification method. This method can effectively extract the morphological characteristics of EEG signals and the cooperative discharge features between different channels. Through the fusion of multiple features of multi-channel EEG signals, the classification performance of epileptic EEG signals has been further improved. This conclusion also proves that considering the cooperative discharge features of multi-channel EEG signals at the same time helps to improve the performance of epilepsy classification. The end-to-end multi-feature fusion deep learning classification model designed in this paper can provide help for clinicians.

关键字 EEG, deep learning

分类：18. Neurology 神经
1239

The Recurrent PACS2 Heterozygous Missense cause Developmental and epileptic encephalopathies by inhibiting GABAergic networks

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Objective Phosphofurin acidic cluster sorting protein 2 (PACS-2) is a multifunctional protein mainly expressed in brain. Children carrying the recurrent heterozygous missense variant of PACS2 Glu209Lys exhibit the characterized developmental and epileptic encephalopathies (DEEs) phenotype. The present study aimed to expand the clinical features with 4 Chinese patients and elucidate the pathogenic mechanism of the recurrent PACS2 missense mutation.

Methods Clinical and developmental information was collected from the patients with PACS2 Glu209Lys under the informed consent. The role of PACS2 in embryo development was investigated by knockdown of PACS2 with antisense MO in zebrafish. Mouse neuroblastoma cells (N2A) were used to study the cellular function of PACS2 as well as the pathogenic mechanism of p.Glu209Lys variant in vitro.

Results
We added 4 unrelated Chinese children who carry heterozygous mutation in PACS2 at locus of Glu209Lys, which confirm the pathogenicity of the hot-spot heterozygous missense mutation. Knockdown of PACS2 in zebrafish embryos induced an epileptiform-like electrographic activity companied with a phenotype of aberrant brain organogenesis. The affected embryos displayed increased neural cell apoptosis and subsequent ventricle enlargement. The phenotype was partially rescued by coinjection with human PACS2 mRNA, but not mutant (Glu209Lys). Follow up transcriptomic analysis in PACS2 MO injected embryos indicated abnormal neurodevelopmental pathways and disturbed GABA network. Strikingly, exogenous GABA could also compensate for some of the epileptiform-like phenotype in the PACS2 knockdown morphants. Similarly, knockdown of PACS2 in N2A cells also exhibited a reductive GABA content.
Conclusions The pathogenic Glu209Lys variant in PACS2 could disturb GABAergic networks and cause the neurodevelopmental disease, which might provide experimental evidence for clinical therapy for patient with this hot-spot mutation.

关键字 Pacs2; Developmental and epileptic encephalopathies; GABA pathway; zebrafish

分类：18. Neurology 神经
1240

Graph Representation of Spike and Slow Waves in the Detection of Absence Epilepsy

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Background
Absence epilepsy is one of the most common types of epilepsy. Clinically, the diagnosis of absence epilepsy is one of the major challenges faced by doctors. Because it lacks the easily observed symptoms (such as convulsions and convulsions) that exist in conventional epilepsy, and it is highly dependent on the detection of spike and slow waves in the brain electrical signal. This is a time-consuming and laborious task for doctors. The introduction of artificial intelligence algorithms to automatically identify spike and slow waves is a promising strategy. However, the morphology of spike and slow waves varies greatly among patients. This brings great challenges to the automatic identification of spike and slow waves. For this reason, accurate identification of spike and slow waves requires a description of the detailed features of the waveform.
Methodology
Recently, graph representations called complex networks have been increasingly used to characterize one-dimensional EEG signals. However, existing methods usually cannot effectively represent spike and slow waves, and it is difficult to capture the differences between the spike and slow waves waveform and its non-spike and slow waves counterparts, such as small differences and different shapes. The existing methods have a very sparse representation of the EEG signal, which loses many details of the EEG signal. To solve this problem, in this work, we propose two simple and effective complex networks, Overlook Graph (OG) and Weighted Overlook Graph (WOG), which have been customized to represent spike and slow waves[1].
Results
A large number of experiments on real absence epilepsy EEG data sets show that the proposed OG/WOG method can accurately represent spike and slow waves. The experiment of reconstructing the EEG signal represented by the graph on the absence epilepsy dataset further shows that our method can restore more detailed information in the spike and slow wave.
Conclusions
We design a graph representation that accurately represents the EEG signal. This graph representation can effectively represent the details of the EEG signal. The performance of this method in real clinical absence epilepsy data is obviously due to the existing graph representation method. This shows that our graph representation method OG/WOG has a highly competitive performance on the task of spike and slow wave detection.
Referrence
[1] Wang J, Liang S, Wang Y, et al. A Weighted Overlook Graph Representation of EEG Data for Absence Epilepsy Detection[C]//2020 IEEE International Conference on Data Mining (ICDM). IEEE, 2020: 581-590.

关键字 Graph representation, EEG

分类：18. Neurology 神经
1261

Clinical characteristics, disease course, and outcomes of paediatric patients with myelin oligodendrocyte glycoprotein-Ab associated disease: A retrospective clinical study

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Abstract
Objective: To delineate the outcomes of paediatric patients with myelin oligodendrocyte glycoprotein antibody disease (MOGAD).
Methods: We retrospectively analyzed the clinical characteristics, treatment, and outcomes of 34 paediatric patients with MOGAD from July 2015 to January 2020.
Results: The median age at disease onset was 75.5 months (range: 19–170 months). The female-to-male ratio was 1:1.1. The median follow-up duration was 34.5 months (range: 14–63 months). Acute disseminated encephalomyelitis (ADEM) was the most common initial phenotype (52.9%), followed by optic neuritis (ON) (20.6%). Children with ADEM were younger than those with ON (P=0.045). Twenty-eight (82.4%) and 18 (56.3%) children had abnormal brain and spinal magnetic resonance imaging, respectively, during the first acute attack. MOG-abs titers in children with ON were statistically higher than those in children with ADEM (P=0.04). Thirty-two children accepted glucocorticoid treatment, while 33 (97%) children demonstrated clinical improvement within 1 week, 21 children (61.8%) achieved clinical recovery within 1 month. Eight children (23.5%) suffered a relapse, the median interval between the initial attack and recurrence was 13 (range: 3–36) months. We detected neurological sequelae in seven (20.6%) children, with visual dysfunction being the most common sequela (85.7%).
Conclusion: ADEM was the most common phenotype in both monophasic and relapsed paediatric MOGAD, followed by ON. Majority of pediatric MOGAD patients were highly responsive to glucocorticoid. Despite a benign prognosis in most patients, some patients endure neurological sequelae, mainly visual impairment. Patients with initial visual impairment should be carefully evaluated and administered individualized immunotherapy.

关键字 myelin oligodendrocyte glycoprotein; MOG; MOG-abs; MOGAD; paediatric

分类：18. Neurology 神经
1311

MT-ND5 Mutation Exhibits Highly Variable Manifestations at Low Mutant Load: a case and review

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Case presentation：a 14-year-old male patient，was asymptomatic until the age of 11, when he developed epileptic seizures and still had seizures under oxcarbazepine and levetiracetam treatment. The seizures manifested as sleep-stage tonic-clonic seizures, which occurred once in two months. He bilateral sensory deafness gradually appeared. In the past year, the visual acuity of both eyes has decreased, the memory and cognitive functions have decreased, and the personality has been autistic. The birth history and past history of the child are normal. The mother had two suspicious convulsions 7 years ago and this year. He is 145cm tall and weighs 30Kg. Electroencephalogram: during awake period, the main spine/spine-slow wave bursts are frequently seen in the frontal-frontal, occipital and temporal areas on both sides of the forehead-frontal side; during sleep, occasionally the right forehead-frontal, occipital and central spine- Slow wave release. Abnormal signals in the right occipital lobe of head MRI, signs of mild atrophy of cerebellum.The whole-genome examination did not detect pathogenic mutations related to clinical manifestations. Genetic testing MT-ND5 m. 13513 G>A, p. D393N and blood mutational load with 12.4%, and ACMG mutation classification 1 type determined to be pathological.
His mother blood mutational load was 5.1%; currently using OCX, LEV, arginine, L-carnitine treatment.
Review the Cochrane central register of controlled trial, Embase and ovid Medline database, remove duplication and include 137 articles, and finally include 77 original documents after reading the abstract and full text. A total of 119 patients with MN-DT5 gene mutations, of which Leigh syndrome (LS) is the most 32 cases, followed by Leber Hereditary Optic Neuropathy (LHON) in 12 cases, mitochondrial encephalopathy, lactic acidosis, stroke-like episodes (MELAS) in 10 cases, MELAS/LS Overlap Syndrome in 10 cases, and cardiomyopathy in children with mitochondrial disease in 6 cases (Cardiomyopathy in children with mitochondrial disease 4) Cases, 1 case of myocardial infarction, 1 case of late onset cardiomyopathy), 3 cases each of adult-onset kidney disease and childhood mitochondrial encephalomyopathies, 2 cases each of maternally inherited diabetes and deafness, Schizophrenia and NAFL syndrome, and the others include LHON/MELAS, SCA/MELAS, ataxia, parkinson disease, mitochondrial genetic variants identified to be associated with posttraumatic stress disorder,high altitude pulmonary edema, type 2 diabetes, multisystemic disorder with renal, endocrine, ocular and hematological involvement and very mild neurological symptoms, intercellular heteroplasmy and rapid shifts between generations , POLG-related mitochondr ial disease, neuromuscular(NM) symptoms, autism, expanded nomenclature, mitochondrial cerebellar ataxia, renal failure, neuropathy, and encephalopathy (MCARNE), mitochondrial calcium Handling defects, lead occupationally exposed lead subjects, mitochondrial respiratory chain enzyme (MRCE), age- related macular degeneration patients, isolated or combined oxidative phosphorylation system deficiency, the other expands the phenotypic spectrum of MT-ND5 mutations beyond Leigh syndrome, MELAS, and optic atrophy, mesial temporal lobe epilepsy patients with hippocampal sclerosis, epithelial-myoepithelial carcinoma of salivary glands , rheumatoid arthritis, MT-ND5 also had a high incidence of secondary mutations,

congenital hyperlactataemia and leigh syndrome, mutational screening in patients with profound sensorineural hearing loss and neurodevelopmental delay.Among them, m.13513 G>A p.D393N has the most mutation sites, 33 cases (27.7%).
Conclusion: the clinical phenotype of MT-ND5 is widespread, including nervous system, kidney, cardiovascular, endocrine, immune, etc., and can also be manifested as cancer.

关键字 MT-ND5， Variable Manifestations， case

分类：18. Neurology 神经
1417

CAPOS syndrome：A new case report originated from acute disseminated encephalomyelitis and literature review

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Background: As a rare autosomal dominant disease, CAPOS syndrome is accompanied with cerebellar ataxia, areflexia, pes cavus, optic atrophy, and sensorineural hearing loss, and is related to ATP1A3 gene mutation. Fifty-five patients have been reported so far, characterized by recurrent acute ataxia and other neurological symptoms in early childhood due to febrile illness. CAPOS syndrome can be relieved in a short time but has long-term neurological sequelae.
Methods: Here we describe a new patient diagnosed with CAPOS syndrome.
Result: The patient presented with acute-onset ataxia, encephalopathy, and sensorineural hearing loss, induced by febrile illness was described. At the same time, abnormal signal on nervous system magnetic resonance imaging (MRI) was found in the patient thus he was diagnosed with acute disseminated encephalomyelitis (ADEM). Then a c.2452G>A mutation in the ATP1A3 gene was identified and CAPOS syndrome was confirmed as well. Conclusions: This is the first case of CAPOS with ADEM onset reported so far. With the development of genetic diagnostic technology, the diagnosis time of CAPOS syndrome is significantly advanced. For children with fever-include ataxia and diseases related to ATP1A3 gene should be considered. However, there is few knowledge about the treatment of the disease and further research are needed.

关键字 CAPOS syndrome; Children; Cerebellar ataxia; Hearing loss; ATP1A3 gene

分类：18. Neurology 神经
1423

Long-term exposure to environmental levels of oxytetracycline potentially leads to neurobehavioural disorders

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Background
As a feed additive in agriculture, the antibiotic oxytetracycline (OTC) has become widely distributed in the natural environment, leading to the exposure of many organisms to low doses of OTC. Studies revealed that OTC potentially impairs thyroid function, which may affect neurobehaviour; however, the impact of exposure to environmental concentrations of OTC on adult neurobehaviour is unknown.

Method
In this study, adult zebrafish were exposed to OTC at environmentally relevant concentrations for 30 days. We investigated the effects of OTC on the thyroid endocrine system in zebrafish, through determinations of thyroid-related hormone and neurotransmitter levels by enzyme-linked immunosorbent assay, and analysis of the mRNA expression of regulatory genes related to thyroid hormones and neurotransmitter using quantitative real-time polymerase chain reaction. In addition, we conducted locomotion test, vibrational-evoked response test, light-dark preference test, and black/white preference test on zebrafish.

Results
In this study, after exposure to OTC for 30 days, the total swimming distance of zebrafish was significantly increased under vibration and light/dark stimulation, while time spent in the white area was prolonged during the black/white preference test, indicating that the zebrafish became bolder and more impulsive under low OTC exposure. Additionally, monoamine neurotransmitter (5-hydroxytryptamine, dopamine, norepinephrine) levels were decreased and gene expression of monoamine oxidase (mao) involved in neurotransmitter metabolism was upregulated at the transcription level after OTC exposure. Because triiodothyronine (T3) levels were enhanced following exposure to OTC, we speculated that T3 may mediate OTC damage to the nervous system. Our simulated molecular docking analysis showed that OTC combined with the sodium iodide cotransporter protein may result in excessive T3 synthesis. We further exposed zebrafish to T3, and they exhibited similar behaviour to the OTC exposure group.

Conclusions
In conclusion, environmental OTC may activate monoamine oxidase and enhance the metabolism of monoaminergic neurotransmitters via T3, thereby inducing abnormal neurobehaviour.

关键字 Antibiotic exposure, Oxytetracycline in the environment, Behaviour change, Neurotransmitter, Thyroid disruption.

分类：18. Neurology 神经
1425

GABRB3-related epilepsy: novel variants, clinical features and therapeutic implications

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Objective: This study aimed to comprehensively examine the genetic and phenotypic aspects of GABRB3-related epilepsy and to explore the potential prospects of personalized medicine.
Methods: Genetic testing was conducted in all epilepsy patients without acquired factors for epilepsy. Through the collaboration of multicenter in China, we analyzed the genotype-phenotype correlation and antiepileptic therapy of 26 patients with GABRB3-related epilepsy.
Results: Thirteen GABRB3 variants were novel, and 25 were de novo. The seizure onset age ranged from 1 month to 21 months (median age: 3.75 months). Seizure types predominated including focal seizures (92.3%), generalized tonic-clonic seizures (23.1%), and epileptic spasms (15.4%). Clinical features included cluster seizures (80.8%), fever sensitivity (53.8%), and developmental delay (96.2%). Neuroimaging was abnormal in 10 patients, including dysplasia of the cerebral cortex, dysplasia of the frontal and temporal cortex, delayed myelination, and corpus callosum dysplasia. Eleven patients were diagnosed with developmental and epileptic encephalopathy (DEE), four with West syndrome, three with epilepsy of infancy with migrating focal seizures (EIMFS), one with epilepsy with myoclonic-atonic seizures (EMAS), one with Dravet syndrome, and one with febrile seizures plus (FS+). Seizures were controlled in 57.7% of patients by valproate, levetiracetam, or perampanel in the majority.
Conclusions: The clinical features of GABRB3-related epilepsy included seizure onset in early infancy, cluster seizures and fever sensitivity. Most patients manifest severe epilepsy phenotypes. Valproate, levetiracetam and perampanel seem to have positive effects on seizure control for patients with GABRB3 variants.

关键字 GABRB3; epilepsy, infancy, seizure cluster, developmental delay

Category: 18. Neurology 神经
1460

HLA alleles in Thai Children with Anti-NMDAR Encephalitis

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Abstract Content Background: Anti-NMDA receptor encephalitis (Anti-NMDARE) is the most common autoimmune encephalitis in children characterized by a complex neuro-psychiatric syndrome and presence of CSF antibodies against the GluN1 subunit of the NMDA receptor. This study is aimed to identify HLA alleles associated with anti-NMDARE in Thai children.

Methods Method: This is a cross sectional study performed at Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, and Department of Pediatrics, Queen Sirikit National Institute of Child Health and collaborate with Department of Medical Science, Ministry of Public Health, Thailand. All Thai patients with diagnosis of Anti-NMDARE between January 2010 and December 2020 were enrolled. Data collection included demographic data, presenting symptoms and signs, CSF analysis, associated tumor, treatment and response were collected. DNA was extracted from peripheral blood leucocytes and HLA genotypes were determined using reverse sequence-specific oligonucleotide probes hybridization. HLA genotypes were compared to the database of 101 Thai children healthy controls.
Results Results: A total of 34 patients enrolled (Female: male 29:5) with mean age 9.25± 4.4 years. The clinical presentations were speech problems, movement disorder, psychological condition, sleep wake disturbance and seizures at 79%, 76.5%, 67%, 58.8% and 55.8%, respectively. Associated tumors were noted in 4 patients (11.8%). Seventeen patients (50%) had HLA DRB1*15:02 positive (16 heterozygous, 1 homozygous). HLA DRB1*15:02 was significantly increased in Thai children with Anti-NMDARE, compared to Thai children healthy controls with allele frequency of 0.265 vs 0.134 (OR 2.32, 95% CI 1.11 to 4.80, P 0.023). Regarding relapse rate, two (11.8%) patients with HLA DRB1*15:02 positive had one clinical relapse. Six (35.3%) patients with HLA DRB1*15:02 negative had clinical relapse, of which 3 had three episodes of relapse.
Conclusion Conclusions: HLA DRB1*15:02 was significantly associated with Anti-NMDARE in Thai children. Patients with HLA DRB1*15:02 positive trended to have less relapse.

Key words Anti-NMDA receptor encephalitis, HLA, Thai Children, autoimmune encephalitis
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Category: 18. Neurology 神经
1470

Reactogenicity and Immunogenicity of the COVID-19 Vaccines BNT162b2 and Sinovac-CoronaVac in Patients with Hereditary or Acquired Neuromuscular Disorders on Immunomodulatory Therapies

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Abstract Content Autoimmune neuropathies and neuromuscular disorders (NMDs) are a group of neurological diseases that can cause disability or even premature death (1). Immunomodulating therapies, such as long-term intravenous immunoglobulins (IVIG) and corticosteroids, are effective in preserving muscle strength for some neurological disease subtypes, including chronic inflammatory demyelinating polyneuropathy (CIDP) and Duchenne muscular dystrophy (DMD). However, undesirable side effects of prolonged treatment include susceptibility to severe infections and reduced immune response to vaccination (2). As such, data regarding the safety and efficacy of the novel COVID-19 vaccines in this group of patients are lacking. In this study, we aim to assess the reactogenicity and immunogenicity of the BNT162b2 mRNA and inactivated virus Sinovac-CoronaVac COVID-19 vaccines in patients with CIDP and DMD.

Methods This prospective COVID-19 Vaccination in Adolescents (COVA) study was approved by the University of Hong Kong (HKU)/HK West Cluster Institutional Review Board (UW21-157). Patients in the age range 11-17 years old with confirmed neurological disease diagnosis and managed with long-term corticosteroids or IVIG were recruited from the Queen Mary Hospital Paediatric Neurology Clinic and the HKU Hong Kong NMD patient registry after informed consent and assent. Advertisements to healthy children and adults as controls were sent to schools throughout the entire territory of HK. Patients could choose between BNT162b2 or Sinovac-CoronaVac. Participants were monitored for at least 30 mins after each injection. Electronic diaries with daily reminders were sent to participants to report adverse events for the 7 days of post-vaccination. Blood was obtained 3-4 weeks after each vaccine dose to measure the IgG antibody levels against the SARS-CoV-2 receptor-binding domain of the spike protein by ELISA. The antibody levels were considered positive if OD450 was above the threshold value of 0.50.

Results Seven DMD patients receiving corticosteroids regularly and 1 CIDP patient on IVIG long-term from the registry were contacted. Three DMD patients declined to join due to personal preferences, while five patients with DMD (n=4) and CIDP (n=1) were enrolled. The dosage range of prednisolone was 0.36-0.7 mg/kg/day for DMD patients. The IVIG dose was 2 grams/kg every 3-4 months for the participant with CIDP. All were male, ages 12 to 15 years old. Three participants received BNT162b2 and 2 received the Sinovac-CoronaVac vaccine. There was no vaccine-related severe adverse event or hospital admission during the 30 minutes observational period or according to their 7-days diaries. All three BNT162b2 recipients experienced pain at the injection site and fatigue. Mild myalgia was the second most common side effect for BNT162b2. On the other hand, 1 patient in the Sinovac-CoronaVac group experienced moderate headache. When compared to the 1st dose, there were higher frequencies of side effects reported

in their diaries after receiving the 2nd dose for both COVID-19 vaccines, which included headache (1 vs 3), fatigue (2 vs 3), nausea (0 vs 1) and cough (0 vs 1). The full set of serology data are pending and should be available by the time of the ASPR conference.
Conclusion Adolescents with hereditary or acquired neuromuscular disorders on regular immunomodulating therapy tolerated both the BNT162b2 and Sinovac-CoronaVac without severe complications. These findings support the safety of COVID-19 vaccination in patients with CIDP and DMD.

Key words COVID-19, Vaccines , Neuromuscular Disorders
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分类：18. Neurology 神经
1471

Application of QCC to improve the quality of written reports of medical record, following neurophysical examination

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Objective: Test the effectiveness of a quality control circle (QCC) of improving the quality of written reports of medical records, following neurophysical examination.
Methods: Subjective and objective approaches were adopted to achieve QCC. Objective methods involved environmental intervention in which the placement of items was standardized, and the number of companions was defined and reasonably allocated to new patients. Subjective approaches included the introduction of doctor intervention methods, improvement the importance of doctors to specialist examination, improvement the children and family intervention methods, and development of guidelines detailing the knowledge of physical examination explain to family members the importance of the procedure.
Results: The quality of written reports of medical records were evaluated using XXX standards. Reports live up to XXX standards were deemed as pass. The pass rate of physical examination reports was 6.03% at the beginning of the trial. After QCC was established, the pass rate of the reports increased to 68.25%.
Conclusion: The use of QCC improved the pass rate of written reports of neurophysical examination.

关键字 neurophysical examination; physical examination report; QCC

分类：18. Neurology 神经
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The regulatory mechanism of type A potassium channel and its effect on body temperature regulation

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A-type potassium channels are voltage gated potassium channels, which is widely distributed in various types of neurons, which mediated the IA current with fast inactivation, rapid activation, 4-AP sensitive characteristics. A-type potassium channel is an important ionic basis of PO/AH neuron warm sensitive properties. There are five subtypes of A-type potassium channel in mammalian neurons, which are Kv1.4, Kv3.4, Kv4.1, Kv4.2, Kv4.3. The Kv4 channel is considered to be the main channel moleculer which mediated IA currents, and the research on the composition and regulation of the Kv4 channel is also in the further development. In recent years, it is found that IA has a closely relationship with the regulation of the body temperature and some physiological functions.

关键字 A-type potassium channels、Accessory subunits、Regulatory mechanism、Body temperature

分类：18. Neurology 神经
1804

Protective effects of TAT-GluA2CT interference GluA2/TARP γ-8 coupling on nerve injury in status epilepticus model at different time points

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Protective effects of TAT-GluA2CT interference GluA2/TARP γ-8 coupling on nerve injury in status epilepticus model at different time points

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【Abstract】Objective To investigate the optimal administration time of TAT-GluA2CT in the protection of nerve injury after epilepsy. Methods Male SD rats(72 cases)were induced to status epilepticus by using LiCl-pilocarpine, while a control group (n = 12) was established. The 72 rats were divided into epilepsy group(n = 12), the TAT-sham peptide group (n = 12), the TAT-GluA2CT peptide group (n = 48) groups according to the random number table method, and the TAT-GluA2CT peptide group were further divided into the previous 1 h group (n = 12), the last 2 h group (n = 12), the last 4 h group(n = 12), and the last 6 h group(n = 12) groups according to the administration time of the TAT-GluA2CT peptide. Nissl staining and TUNEL assay were performed on 6 rats each from the control group ,epilepsy group, the TAT-sham peptide group, the previous 1 h group, the last 4 h group, and the last 6 h group to observe the morphological changes and apoptosis of neurons in the CA1 region of the rat hippocampus. Western Blot and Co-IP test were used to detect the expression of GluA2 and the coupling of GluA2/TARP γ-8 complex in control group, epilepsy group, the previous 1 h group, the last 4 h group, and the last 6 h group. Result Compare with epilepsy, the number of nerve cells in each TAT-GluA2CT peptide group was significantly increased and the number of apoptotic cells decreased significantly after the application of interfering peptide ($p<0.01$). Compared with the control group, the expression of GluA2 in each interferon group decreased, and the difference was statistically significant ($p < 0.01$). There was no significant difference in the expression of GluA2 between each interferon group and epilepsy group ($p > 0.05$). Compared with the epilepsy group, the coupling of GluA2/TARP γ-8 complex in each interferon peptide group was significantly lower than that in the epilepsy group, and the seizure latency was prolonged and the seizure rating was decreased in the previous 1 h group compared with the epilepsy group, the difference was statistically significant ($p < 0.01$). Conclusion The application of interfering peptide TAT-GluA2CT can reduce the injury of hippocampal neurons in epileptic rats,and the optimal administration time of TAT-GluA2CT is 1 hour before or 2 hours after pilocarpine administration.

关键字 status epilepticus; α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptor ; TARPs; GluA2/TARPγ-8 complex

Child Health Care & Developmental Behavior

儿童保健与发育行为

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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新生期反复操作性疼痛对婴幼儿大脑结构及功能的不良影响

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Background A large number of studies have confirmed that repeated painful operations experienced in the neonatal intensive care unit (NICU) will not only cause immediate stress response in newborns, but also affect the cognitive, emotional and sensory development of infants and young children. Clinical follow-up studies have found that more operations in the neonatal period will lead to poor learning ability in preterm infants during school age and a higher risk of chronic generalized pain in childhood and adulthood, but the relevant mechanism is still unclear. Cognitive and emotional behaviors are closely related to brain development. In recent years, the newly developed functional magnetic resonance imaging technology including diffusion kurtosis imaging (DKI), can give in-depth analysis of the development and maturity of the microstructure of brain, providing a basis for studying the adverse effects of pain experience on brain development during the critical period of life.
Method Premature infants who were hospitalized in the NICU of the Children's Hospital of Nanjing Medical University after birth were included. The clinical information during the hospitalizations in NICU were collected, especially the number of painful operations. At the age of 1 year, follow-up on physical, cognitive, and emotional development and functional magnetic resonance testing were performed. Physical assessment mainly includes indicators such as height, weight, and head circumference. The Gesell Child Development Scale was used to evaluate infants' motor, language, adaptability and social skills. A revised version of the Infant Temperament Questionnaire was used to assess infant emotional development. The 3.0T magnetic resonance imaging system is used to obtain high-resolution T1-weighted imaging and T2-weighted imaging under conventional scanning, and perform diffusion kurtosis imaging (DKI) detection. We quantitatively analyzed mean kurtosis (mean kurtosis, MK), kurtosis fractional anisotropy (kFA) and other indicators mainly reflecting the degree of maturity of brain gray matter. Correlation analysis was made between the number of painful operations, behavioral emotional development and brain maturity.
Result After controlling for clinical risk factors, the number of neonatal painful experiences during NICU hospitalization was significantly negatively correlated with the developmental quotient assessed by Gesell ($P<0.05$) and fitness scores in the temperament scale ($P<0.05$). Greater neonatal invasive procedures were associated with lower volume in gray matter ($P<0.01$), less values of MK in the areas of right anterior cingulate and left medial superior frontal gyrus, less values of kFA in the areas of left anterior cingulate. The reduced values of kFA in the anterior cingulate were associated with decreased personal-social quotient in the developmental test.
Conclusion Neonatal painful procedures are associated with abnormal brain structure and function development at the age of 1 year. It is manifested as a decrease in the volume of gray matter, a decrease in the maturity of the cingulate gyrus and medial superior frontal gyrus, accompanied by a decline in cognitive score development, and poor adaptive temperament development. The results of this study are based on functional magnetic resonance technology, revealing for the first time that early pain experiences may affect the structure and function development of brain in children at the age of 1 year, providing a basis for studying the adverse effects of pain experiences on brain development during the critical period of life. This study

may also provide objective indicators for early clinical screening of brain damage and evaluation of intervention efficacy.

关键字 Neonatal pain, infants, cognition, emotion, functional magnetic resonance

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Comparison of the differences between web-based and traditional questionnaire surveys in pediatrics

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Background: Questionnaire survey is an important method in social science studies. The method was invented in 1930s and has been widely adopted in psychological studies. With the advent of technology, web-based survey has been appreciated as a novel method, and has been applied in clinical studies. Although previous studies have shown that the accuracy of the web-based survey may be higher, it is primarily used in basic information collection, satisfaction survey and marketing. Besides, findings from fields related to subjective cognition have been shown to be highly vulnerable to survey methods. In pediatrics, the subjects of questionnaire survey are mainly caregivers, who are often subjective, thus the adopted survey methods might yield varying data. Whereas some studies have applied web-based survey in pediatrics, data on the differences between the web-based and traditional questionnaire surveys remain scant.

Objective: The objective of our study was to evaluate the internal consistency of web-based survey and to compare it with traditional questionnaire survey in pediatrics.

Methods: A convenience sample of caregivers were invited to participate in the survey on the feeding patterns and their children's eating behavior if their children were aged 2 to 7 years. A web-based survey and a traditional questionnaire survey were carried out between October 2018 and July 2019. The web-based survey was set as an open survey, and was promoted remotely through WeChat on the internet (web source) as well as paper posters in the child health care clinic (hospital source). The traditional questionnaire survey was mainly conducted by face-to-face questioning. The sample size was calculated using a single proportion sample size estimating algorithm. A total of 1085 caregivers were involved in this study, and they were divided into 3 groups based on the methods and sources: (1) web-based survey from web source, (2) web-based survey from hospital source, (3) traditional questionnaire survey from hospital source. The data were then compared and analyzed. Descriptive statistical tools were used to analyze demographic characteristics of the subjects. We used ANOVA and LSD test to compare the feeding patterns. On the other hand, comparison of the eating behavior problems was carried out by chi-square test. Bonferroni correction was utilized for multiple comparisons. $P<.05$ was considered statistically significant.

Results: A total of 735 caregivers participated in the web-based survey and 350 caregivers participated in the traditional questionnaire survey, and 816 cases were then included in the analyses after data processing. The effective rate of the web-based survey was 70.1% and the completeness rate of the traditional questionnaire survey was 86.0%. The data showed that there were no significant differences between web-based surveys from different sources. But the demographic characteristics between the web-based and traditional questionnaire surveys were significantly different, mainly in age and caregivers ($P=.002$ and $P<.001$). Age-specific stratified analysis then showed the scores of feeding patterns and reporting rates of eating behavior problems were significantly higher in the web-based survey compared to the traditional questionnaire survey, mainly in the younger age group after adjusting for demographic characteristics.

Conclusions: Taken together, our study demonstrated that web-based survey could be a feasible tool in pediatric studies. However, differences in demographic characteristics and their possible impact on the results should be considered in the analyses.

关键字 pediatrics, surveys and questionnaires, web survey

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Clinical characteristics of catch-up growth in small for gestational age infants

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Objectives:
This study aims to observe the clinical characteristics of catch-up growth in small-for-gestational age infants, and provides scientific basis for evaluating the growth and development of small for gestational age children and promotes the healthy growth of small for gestational age children.
Methods:
This study included small-for-gestational-age infants who visited and followed up at the Outpatient Clinic of the Children's Health Department of Nanjing Children's Hospital from June 2019 to December 2020 (evaluation criteria: according to fenton-2013 growth curve, birth weight and/or length lower than the 10th percentile of the average weight and/or length of the same gestational age and sex.). And exclude twins, congenital dysplasia, hypothyroidism, long-term use of hormones and other drugs that affect growth. The included infants smaller than gestational age were divided into Catch-up growth (CUG) and Non catch-up growth (NCUG) groups according to whether the SDS of weight and/or length increase was greater than 0.67.Perform physical assessments for children who meet the inclusion criteria, including body length, weight, and head circumference, and calculate the body mass index (BMI) [Formula: BMI = body weight (kg) / body length (m)2]. According to the World Health Organization child growth standard (2006), the z scores of children's weight, body length, head circumference, and BMI were calculated. For premature babies within 1 year of age, Z score conversion is performed after correcting gestational age.Development screen test (DST) (School of Pediatrics, Fudan University, 2007) was used to test the areas of motor ability, social adaptation ability and intelligence ability respectively.And detect related indicators: blood sugar, albumin, prealbumin, blood creatinine, triglycerides, and serum IGF-1 and IGFBP-3 quantitatively.The independent sample t test was used for comparison between the two groups, the Mann-Whitney U test was used for non-normal distribution; the chi-square test was used for the comparison of categorical variables between groups.
Results:
A total of 169 small for gestational age infants were included in this study, including 72 cases (42.6%) in CUG group and 97 cases (57.4%) in NCUG group.The length Z-score of CUG group was significantly higher than that of NCUG group from 6 months old (all $P < 0.001$), the weight Z-score was significantly higher than that of NCUG group from 3 months old (all $P < 0.05$), the Z-score of head circumference was significantly higher than that of NCUG group from 1 month old (all $P < 0.001$), and the Z-score of BMI was significantly higher than that of NCUG group from 3 months old (all $P < 0.05$). The growth rate of CUG group reached the peak before 6 months of age, and reached the catch-up growth standard ($\triangle Z > 0.67$).
The neuropsychological development scores, blood glucose and insulin-like growth factor-1 (IGF-1) levels of small-for-gestational infants in the CUG group were higher than those in the NCUG group (all $P<0.05$).
In addition, at the age of 3 and 6 months after birth, the Z-scores of length, weight and BMI of infants fed with fortified nutrition formula in the CUG group were higher

than those of exclusive breastfeeding (all P＜0.05), and there was no significant difference in Z-scores of head circumference (all P>0.05).
Conclusions：
The postnatal physical growth rate, neurodevelopment level, blood sugar and blood IGF-1 levels of smaller than gestational age children with catch-up growth are significantly higher than those without catch-up growth. Six months after birth is the peak of catch-up growth. In children with catch-up growth, nutritional supplementation formula feeding can promote body length and weight to catch-up growth faster and increase body mass index.

关键字 Small for gestational age; Catch-up growth; Clinical characteristics

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Factors related to catch-up growth in small for gestational age infants——An analysis of 169 clinical cases of small for gestational age infants

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Objectives:
To explore the factors that influence the catch-up growth of small-for-gestational-age infants after birth, and to provide a scientific basis for improving the prognosis and promoting the healthy growth of small-for-gestational age infants.
Methods:
This study included small-for-gestational-age infants who visited and followed up at the Outpatient Clinic of the Children's Health Department of Nanjing Children's Hospital from June 2019 to December 2020 (Evaluation criteria: according to fenton-2013 growth curve, birth weight and/or length lower than the 10th percentile of the average weight and/or length of the same gestational age and sex.). And exclude twins, congenital dysplasia, hypothyroidism, long-term use of hormones and other drugs that affect growth. The included infants were divided into Catch-up growth (CUG) and Non catch-up growth (NCUG) groups according to whether the SDS of weight and/or length increase was greater than 0.67.An unified questionnaire was used to collect the clinical characteristics of small for gestational age infants during fetal period and delivery, as well as personal information such as their feeding history and disease history after birth. Calculate the birth weight index (PI) [Formula: PI = weight (g) / length (cm) 3×100].Perform physical and nutrient intake assessments for children who meet the inclusion criteria.The independent sample t test was used for comparison between the two groups, the Mann-Whitney U test was used for non-normal distribution; the chi-square test was used for the comparison of categorical variables between groups. Multivariate unconditional Logistic regression analysis was used.
Results:
A total of 169 small for gestational age infants were included in this study, including 72 cases (42.6%) in CUG group and 97 cases (57.4%) in NCUG group. The gestational age, birth weight and PI value of CUG group were lower than those of NCUG group (all P < 0.05), and the proportion of neonatal disease history, mother's height and total monthly family income of CUG group were higher than those of NCUG group (all P < 0.05); The proportion of mothers with a history of gestational hypertension in CUG group was higher than that in NCUG group (P < 0.05), while the proportion of mothers with a history of progesterone use in CUG group was lower than that in NCUG group (P < 0.05). There was no significant difference between the two groups in the nutritional intake after birth and whether or not to carry out nutrition fortified formula feeding (P > 0.05).Logistic regression analysis showed that after adjusting birth weight and gestational age, PI value at birth was less than 2.5 (OR = 1.894, 95% CI: 1.036-2.575), mother's height was more than 1.55m (OR = 2.017, 95% CI: 1.506-2.827), family monthly income was more than 10000 yuan (OR = 1.882, 95% CI: 1.312-2.466), mother had history of gestational hypertension (OR = 1.793, 95% CI: 1.150-2.561), and no history of progesterone use (OR = 1.937, 95% CI: 1.036-2.575), 95% CI: 1.173 ~ 3.582) were closely related to catch-up growth of small for gestational age infants.
Conclusions：

The body size at birth, the height of the mother, the family income, the history of hypertension during pregnancy and the history of progesterone use are the main factors that affect catch-up growth of small for gestational age children.After birth, nutrient intake and feeding methods have nothing to do with whether catch-up growth can be achieved.

关键字 Catch-up growth; Small for gestational age; Influencing factors

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Relationship between dietary behavior and physical growth in children with Attention deficit hyperactivity disorder

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Objective：The aim of this study was to investigate the dietary behavior in ADHD children aged 4~13 years old and its relationship with growth index and disease-related symptoms.Methods：A total of 548 children and adolescents aged 4-13 years were recruited from the Department of Child Health Care of Children's Hospital of Nanjing Medical University from June 2019 to June 2020. Among them, 396 children met the diagnostic criteria for ADHD in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V). The demographic characteristics and information regarding children’s eating behaviors were collected by self-designed questionnaire and Chinese version of the parent-completed Children’s Eating Behavior Questionnaire (CEBQ). Results:The BMI-SDS（0.10vs0.42）, FM%（17.05%vs19.05%）, the overweight（14.5%vs22.5%）and obesity（8.6%vs13.4%）rate of normal group were lower than ADHD group (P<0.05). There was no statistical difference in the rate of short stature and underweight between two groups (P>0.05). The analysis of CEBQ showed that scores of "slowness in eating" (11.01±3.32vs9.74±2.95), "fussiness" (15.61±3.54vs15.03±2.84), "food responsiveness" (11.96±4.81vs9.88±3.71) and "desire to drink" (8.34±3.46vs6.58±2.72) in the ADHD group were higher than those in the normal group. Mediating effect analysis showed that the relationship between inattention score and FM% in ADHD children was completely mediated by "food responsiveness" (c=0.758, a=0.387, b=0.542, P＜0.05, c’=0.548, P＞0.05). Conclusion: ADHD children have higher rates of overweight and obesity and more dietary behavior problems than normal children. ADHD-related symptoms, eating behavior problems and their fat mass percentage are significantly correlated. Food responsiveness of ADHD children is an important factor connecting ADHD to obesity.

关键字 Attention deficit hyperactivity disorder; Dietary Behavior; Obesity; Food responsiveness; Mediating Effect

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Diagnostic Value of the Diagnostic Receptive and Expressive Assessment of Mandarin-Comprehensive (DREAM-C) in Children's Language Delay or Disorder in Hubei Province, China

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Background: Standardised Mandarin assessment tools for examining deficits in language comprehension and expression at different developmental ages are limited in China. The first comprehensive standardised Mandarin assessment tool is the Diagnostic Receptive and Expressive Assessment of Mandarin-Comprehensive (DREAM-C), which is normed for children aged 2.5–8 years in Mainland China. This study aimed to explore the diagnostic value of DREAM-C in in children with language delay/disorder in pediatric outpatient clinics in Hubei Province, China.
Methods: The detailed medical history of paediatric patients with speech and language problems in child healthcare paediatric outpatient clinics was taken by clinicians and speech-language therapists and assessed using the DREAM-C, Gesell Developmental Schedules (GDS), and Wechsler Preschool and Primary Intelligence Scale (WPPSI-IV) in Tongji Hospital in Hubei Province, China, from December 2018 to January 2020. The sensitivity, specificity, percent agreement and correlation coefficient for three assessments were compared for 320 children with language delay/disorder, 101 children typical children.
Results: The parents of 531 paediatric patients with medical records complained of the following: 362 (68.15%), language delay; 42 (7.91%), hyperactivity and inattention; 43 (8.10%), slurred speech; 37 (6.97%), communication difficulties; 27 (5.08%), language delay accompanied by communication difficulties; and 20 (3.77%), language delay accompanied by slurred speech. Results showed that the sensitivity and specificity of DREAM-C was as high as that of GDS (>0.80) in children with language delay/disorder, and the VCI in WPPSI-IV had a moderate sensitivity (0.58) in differentiating language delay/disorder in the LD group. The percent agreement between the DREAM-C subscales and language DQ of GDS was also high (70.63%-82.81%). The scores of each subscales of DREAM-C had a moderate and significant positive correlation with the language DQ of GDS ($r=0.35-0.56$, $p<0.01$). The scores of each subtest of DREAM-C had a significant low correlation with the verbal comprehension index in WPPSI-IV ($r = 0.27-0.39$, $p < 0.05$) in the LD group.
Conclusions: DREAM-C is a reliable language assessment tool. Its diagnostic value is better than those of GDS and WPPSI-IV in terms of identifying areas where children's language impairments exist. It is more suitable for Chinese children with language delay or disorder. It can help clinicians and speech-language therapists develop an appropriate individual rehabilitation plan for paediatric patients.

关键字 Language delay, Language disorder, Mandarin, DREAM-C

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Effect of Online Parent Training in Promoting Language Development of Children with Language Delay in Hubei Province, China

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Background: Training parents to implement language and communication intervention techniques is an effective approach to promote language development for children with language delay.This study introduces an online parent training program currently conducting in Hubei Province, China, which was designed to help parents of children with language delay with a diagnosis of Autism Spectrum Disorder (ASD), Developmental Language Disorder(DLD) or Global Developmental Delay (GDD) to apply language training techniques into daily interactions and promote their children’s language development at home.
Methods: An online training program was designed to improve the language and communication skills for children with language delay in a naturalistic way. The parents participated a total of 8 hours of online training, including lessons on milestones in child language development, common misunderstandings of child language development, and three basic family language rehabilitation techniques incorporating active learning through videotape analysis and discussion. The course was continued by a three-month online home instruction of all the parents during which the speech-language therapists answered parents' questions on a weekly basis. Gesell Developmental Scale (GDS) was carried out before the online parent training program and after 3-month online home instruction,.
Results: 53 parents and their children aged 12 months to 68 months with language delay participated in the online training program. The results of the GDS assessments conducted before and after the program showed that not only the developmental quotient (DQ) of language improved, but the DQ of fine motor, social behavior and adaptive behavior improved as well ($p<0.05$). Children whose parents utilized strategies of high engagement in “joint attention”, “joint play” and “joint talk” showed significant improvement in the language DQ. However, it does not seem to significantly contribute to improvement in the adaptive behavior DQ, and the personal-social DQ. There is no between group difference of Children diagnosed with Autism Spectrum Disorder and Developmental Language Delay or Global Developmental Delay ($p>0.05$). Furthermore, the quality (parent engagement in applying the three techniques) plays a much more important role than the quantity (time spend with children) of parent-child interaction in improving the child’s language abilities.
Conclusion: The Online parent training focusing on improving daily interaction with their children and speech-language stimulation promoted the development of language skills. It is an economical and practical approach for children with language delay who have limited access to local language intervention programs.

关键字 developmental language disorder, autism spectrum disorder, online parent training, language intervention, Gesell developmental scales.

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Head acupuncture for children with autism spectrum disorders visual auditory information conduction disorders research

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Head acupuncture for children with autism spectrum disorders visual auditory information conduction disorders research

【 Abstract】 Objective To observe the therapeutic effect of acupuncture on autistic audiovisual disorder by randomized controlled study. Methods 60 cases of autistic patients were randomly divided into experimental group and control group, 30 cases in experimental group and 30 cases in control group. Both groups received speech training and special education. The control group did not receive acupuncture, while the experimental group received scalp acupuncture on the basis of the control group. The meridian theory of traditional Chinese medicine was combined with the functional positioning theory of cerebral cortex of modern medicine. The dialectical selection of acupoints (Zhiqi, Zhijiu, Xingan, Broca, visual area, visual contact area, emotional area, Lin's temporal three needles) and body,acupuncture, （eye acupuncture Ear acupuncture) and other acupoints. Choose 30 filiform needles with a length of 25-40mm, take the child's sitting position and fix the head. The doctor can use the single hand push method and the two hand push method. The needle body and scalp form an angle of 15-30 degrees, and quickly enter the needle. The needle will be pushed parallel to the scalp by 0.5-1 inch, and the needle will stay for 2 hours. During the needle retention period, the needle was twisted every 15-20 minutes. Scalp acupuncture and body acupuncture alternate every other day, 15-20 days as a course of treatment, 15-20 days rest between courses of treatment, observe the curative effect after 3 courses of treatment. By comparing the score changes of Gesell test and cars before and after treatment, the total effective rate, significant efficiency and the period of excellent treatment effect were obtained and analyzed. Results before treatment, there was no significant difference in the scores of social adaptation, language, personal social ability area and cars between the two groups (P > 0.05). After treatment, the scores of social adaptation, language, personal social ability area and cars of the two groups were improved compared with those before treatment, and the difference was statistically significant (P < 0.01), The difference was statistically significant (P < 0.05). Conclusion acupuncture can effectively improve the visual and auditory impairment of autism and improve the clinical therapeutic effect。[Key words] autism spectrum disorders ; Acupuncture; Hearing and hearing impairment.

关键字 自闭症谱系障碍 ;针刺；视觉听觉 信息传导障碍。

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Growth of children with biliary atresia before and after liver transplantation

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Objective: To understand the growth of children with biliary atresia (BA) before and after liver transplantation (LT).

Methods: The study included 124 children with BA who were diagnosed and received surgery at the Children's Hospital of Chongqing Medical University from September 1, 2019 to March 31, 2021. The patients were given feeding counseling and oral nutritional supplements, and received follow-up monitoring of weight, length and head circumference after discharged. Then the age-specific standard deviation scores (Z_W, Z_L and Z_{HC}) were calculated by WHO Anthro. Descriptive statistical methods were used to analyze the basic characteristics of the patients, Student's t-test and repeated measures ANOVA were used to analyze differences in Z scores, LSD was used to conduct multiple comparisons, and Spearman correlation test was used to analyze the correlation between ΔZ and liver pathological grade.

Results: (1) 50.0% of the patients were male (62/124), preterm infants accounted for 11.3% (14/124) and small for gestational age infants accounted for 15.3% (19/124). 50.8% of the patients (63/124) could not be contacted due to transfer to other hospital or abandonment of treatment during the follow-up. (2) Z_W at birth was -0.44±1.15, which was significantly lower than the standard mean (t=-4.236, p<.001). Z_W at diagnosis was -0.94±1.05, which was significantly lower than that at birth (t=3.257, p=.001). (3) There were significant differences of Z_W, Z_L and Z_{HC} among diagnosis, 1 month after diagnosis and 2 months after diagnosis (n=22; F=5.400, p=.022; F=8.266, p=.004; F=11.706, p<.001). Multiple comparisons showed Z_W, Z_L and Z_{HC} at 1 month after diagnosis were significantly lower than those at diagnosis (p=.026, .007, .005). Z_L and Z_{HC} at 2 months after diagnosis were still significantly lower than those at 1 month after diagnosis (p=.039, .034). (4) There were significant differences of Z_W, Z_L and Z_{HC} among LT, 1 month after LT, 3 months after LT, 5 months after LT and 7 months after LT (n=17; F=10.874, p=.001; F=5.429, p=.017; F=22.958, p<.001). Multiple comparisons showed Z_W, Z_L and Z_{HC} at 1 month after LT were significantly lower than those at LT (p<.001, p<.001, p<.001). Then Z_W recovered at 3 months after LT and continued to accelerate to a plateau stage at 7 months after LT, Z_{HC} recovered at 3 months after LT and continued to accelerate at 7 months after LT, but there was no accelerated growth of Z_L within 7 months after LT. (5) The ΔZ_L at 2 months after diagnosis was negatively correlated with the liver pathological grade at diagnosis (r=-0.447, p=.048). (6) During the follow-up, there were 39 patients at diagnosis, 25 patients at 1 month after diagnosis and 11 patients at 2 months after diagnosis who completed the dietary records, and there were only 11 patients at diagnosis, 7 patients at 1 month after diagnosis and 4 patients at 2 months after diagnosis whose energy intake reached the recommended level.

Conclusion: BA may increase the risk of intrauterine growth retardation, and the growth rate after birth is still insufficient, especially in linear growth. Chronic liver damage is a related factor of the ΔZ_L before LT. Z_W and Z_{HC} can return to the level of LT at 3 months after surgery, then accelerate in varying degrees, while Z_L does not accelerate at 7 months after LT. The effects of feeding counseling and oral nutritional supplement after diagnosis is not satisfactory, it is necessary to

further strengthen health education, and the feeding methods should be changed if necessary.

关键字 biliary atresia; liver transplantation; growth

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The change of genetic susceptibility in the pathogenesis of food allergy in the past 10 years

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Objective: To investigate the influence of positive family history of allergic diseases on the prevalence rate of food allergy (FA) in children aged 0 to 2 years, and to explore the effect and the change of genetic susceptibility in the pathogenesis of FA from 2009 to 2019.
Methods: The data of two epidemiological surveys on FA in children aged 0 to 2 years in 2009 (n=401) and 2019 (n=513) was analyzed. The participants were divided into two groups according to their family history of allergic diseases, and chi-square test was conducted to analyze the differences of FA prevalence rates.
Results: (1) The total prevalence rates of FA in 2009 and 2019 were 7.7% (31/401) and 11.1% (57/513), respectively. Although the rate increased by 44.2% in the past 10 years, there was no significant difference (χ^2=2.956, p=0.086). (2) The proportions of children with positive family history of allergic diseases in 2009 and 2019 were 28.9% (116/401) and 35.5% (182/513), and the constituent ratios of the two were significantly different (χ^2=4.394, p=0.036). (3) The proportions of FA children with positive family history of allergic diseases in 2009 and 2019 were 45.2% (14/31) and 45.6% (26/57), there were no significant differences (χ^2=0.002, p=0.968). (4) In 2009 and 2019, the prevalence rates of FA in the positive family history group were 12.1% (14/116) and 14.3% (26/182), while 6.0% (17/285) and 9.4% (31/331) in the negative family group. And there were no significant differences in the past 10 years neither in the positive family history group nor in the negative family history group (χ^2=0.300, p=0.585; χ^2=2.465, p=0.116). However, the prevalence rate of FA in the positive family history group was higher than that in the negative family history group in 2009 (χ^2=4.306, p=0.038), but there was no significant difference between the two groups in 2019 (χ^2=2.878, p=0.090).
Conclusion: During the past 10 years from 2009 to 2019, the number of children with positive family history of allergic diseases increased, but the prevalence rate of FA increased slowly and tended to be stable. And the effect of genetic susceptibility in the pathogenesis of FA seemed to be stable and had a decreasing trend.

关键字 food allergy; prevalence rate; genetic susceptibility

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Current situation of common fat soluble vitamins deficiency and evaluation of oral supplement effect in children with biliary atresia in southwest China

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Objective: To investigate the situation and factors of fat soluble vitamins deficiency, evaluate the effect of high-dose oral supplementation of fat soluble vitamins in children with biliary atresia in Southwest China.
Methods: 96 children with biliary atresia were recruited in this study. Collecting basic information, examining biochemical parameters and fat soluble vitamins preoperatively, oral vitamin A 15000IU per day, vitamin D 1000IU per day, and vitamin E 100mg every other day after surgery, monitoring fat soluble vitamins and biochemical indicators before 2 years old or rise to normal levels. Variance analysis, Pearson or Spearman correlation analysis, multiple linear regression and curve regression were used to explore the factors of fat soluble vitamins, the changes of fat soluble vitamins were compared by paired t-test or two independent sample t-test.
Results: 1. The deficiency rate of vitamin A in children with biliary atresia was 38.5%, the marginal deficiency rate was 47.9% and the sufficiency rate was 13.5%; the deficiency rate of vitamin D was 90.6%, the insufficiency rate was 6.3% and the sufficiency rate was 3.1%; Vitamin E deficiency rate was 100%. 2. Total bilirubin ($p=0.048$), indirect bilirubin ($p=0.013$), alkaline phosphatase ($p=0.026$) and liver pathological stage ($p<0.001$) were risk factors for vitamin A deficiency in patients; age ($p=0.003$) and season ($p<0.001$) of diagnosis were risk factors for vitamin D deficiency; risk factors for vitamin E deficiency were age at diagnosis ($p<0.001$) and alkaline phosphatase ($p=0.018$). 3. The relationship between fat soluble vitamins and biliary obstruction related biochemical indicators (total bilirubin, direct bilirubin and alkaline phosphatase) meets the logarithmic function model ($p<0.001$). 4. One month after diagnosis, there was no statistical difference in the changes of vitamin A ($p=0.370$) and D ($p=0.088$) in patients received oral supplementation of fat soluble vitamins, but they were significantly decreased in those without supplementation ($p<0.001$, $p=0.025$), in both patients with and without supplementation vitamin E was significantly decreased ($p<0.001$, $p=0.015$). There was no significant difference in the changes of vitamin A ($p=0.254$), D ($p=0.875$) and E ($p=0.076$) after oral supplementation with 1 month or 2 months. 5. The levels of vitamin A ($p<0.001$), D ($p<0.001$) and E ($p<0.001$) of patient after liver transplantation were significantly increase than before, deficiency rate decreased from 67.4%, 89.1% and 97.8% to 0.
Conclusion: 1. The deficiency rates of vitamin A, D and E in children with biliary atresia were 38.5%, 90.6% and 100%. 2. Vitamin A in patients was affected by liver pathology and indicators of biliary obstruction (total bilirubin, indirect bilirubin, alkaline phosphatase); vitamin D was affected by age and season at diagnosis; vitamin E was affected by age at diagnosis and indicators of biliary obstruction (alkaline phosphatase). 3. Oral supplementation of fat soluble vitamins in patients can slow down the decreasing trend of vitamin A and D, but it is difficult to correct the deficiency. 4. One month after liver transplantation, fat soluble vitamins deficiency of patients can be corrected quickly.

关键字 Biliary atresia, Fat soluble vitamins, Deficiency, Supplementation, Children

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Longitudinal follow-up study on neuropsychiatric development of low birth weight infants of different gestational ages within the age of two years

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Longitudinal follow-up study on neuropsychiatric development of low birth weight infants of different gestational ages within the age of two years

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Abstract: Objective To analyze the neuropsychological development of low birth weight infants in different gestational ages within the age of two years, so as to provide basis for targeted early intervention. Methods From January 2016 to February 2017, a total of 280 low birth weight infants (LBWI) who completed neuropsychological development follow-up within the age of two years in Minhang District of Shanghai were collected. According to gestational age, they were divided into three groups: early preterm (28-33 + 6 weeks, EPT), late preterm infants (34-36 + 6 weeks, LPT) and term infants (37-41 + 6 weeks, T). General movement assessment (GMs) and Gesell scale were employed to evaluate the objects' neurobehavioral development. Results The higher abnormal rate of GMs in preterm birth or torsion stage showed in the lower gestational age group (c2=7.36，P＜0.05)，while no difference was found in the restless movement stage (c2 = 4.36, P > 0.05) . At 9,18 and 24 months'(9 ± 1, 18 ± 2, 24 ± 3 months after birth) ,all of the development quotient (DQ) of the five domains of Gesell scale reached the normal level ,which was more than or equal to 86,except for the five domains at the 9 months and the language ,individual－social at 18 months in EPT group; The lower DQ of the five domains in the lower gestational age group, except for the domains of language and individual－social at 24 months (P < 0.05). The higher rate of developmental delay judged by DQ lower than 86 was found in the lower gestational age group, with statistically significant difference of the three groups in the five domains at 9 months and in the domains of fine motor, adaptability and individual－social at 18 months (P < 0.01). The multiple linear regression analysis indicated that a significantly positively correlation between gestational age and the DQ of all the domains in different age group after adjustment for confounding factors including the children, parents and families, except for the domain of individual－social at 24 months (ß distributed from 0.612 to 2.382, P < 0.01). Conclusion Gestational age is an important independent factor for the

neuropsychological development of LBWI within 2 years old, with the lower gestational age, the worse development. The two preterm groups of EPT and LPT show a catch-up neuropsychological development, and can reach the normal level until 2 years old, while the DQ of the domains of gross motor, fine motor and adaptability are still lower than the T group. we should strengthen the early systematic health of LBWI, especially for the preterm children, in order to realize the early detection and personalized intervention of the developmental delay and promote the early reasonable catch-up and all-around balanced development.

关键字 low birth weight; preterm; term; neuropsychological development; general movement assessment; Gesell

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ICF Based the Analysis of sensory integration training in rehabilitation development of children with low vision

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Abstract:Objective :To explore ICF based the application value of Sensory Integration training in rehabilitation development of children with low vision. Methods: From Octorber 2019 to March 2020, 60 children with low vision were screened in the optometry clinic.According to the random number table method, 60 children were divided into observation group and control group with 30 cases in observation group and control group . The control group used visual aids,while the observation group received Sensory Integration training combined with visual aids.The results were analyzed by using paired-Samples t test.Results: Before training,there were no statistically significant scores of sensory integration scores between the two groups (P＞0.05).After 3 months of continuous intervention, the scores of sensory integration in the observation group were all higher than that in the control group （P＜0.05）. Conclusion: Sensory Integration training combined visual aids could more significantly improve the application effect on quality of live of children with low vision.

关键字 ICF-CY,Sensory Integration training, visual aids, low vision.

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The study of the pathogenesis of idiopathic central precocious puberty based on gut microbiota

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Object To analyze the correlation between gut microbiota (GM) and hyperandrogenemia, insulin resistance, carbohydrate metabolism, and explore whether the pathogenesis of idiopathic central precocious puberty (ICPP) and polycystic ovary syndrome (PCOS) is consistent based on GM.
Methods In this study, we have recruited 27 ICPP (ICPP group) and 23 healthy children (healthy group), and collected the blood and fecal samples from the participants. Blood samples were tested for hormones, including the follicle-stimulating hormone, luteinizing hormone, estradiol, prolactin, and testosterone. DNA was extracted from fecal samples, and amplified and sequenced with 16S rDNA V3-V4 region. Finally, we annotated the sequencing results, counted the differences in hormone indicators and GM composition between the two groups, and analyzed the correlation with clinical indicators. At the same time, we reviewed the literature on GM and PCOS.
Results Compared with the healthy group, the ICPP group exhibited significantly higher levels of the hormone and other indicators ($P < 0.05$). At the phylum level, the ICPP group showed significantly enriched Proteobacteria than the healthy group (4.85% vs 2.92%). At the genus level, the abundances of Roseburia and Prevotella were significantly higher in the ICPP group than those in the healthy group (7.55% vs 2.01%, 3.95% vs 0.19%), but Bacteroides were obviously decreased in the ICPP group (29.96% vs 44.91%). In addition, the potential associations underlying the sex hormonal secretion and the carbohydrate metabolism pathways of GM increased significantly in the ICPP group.
Conclusion The alternations of GM in ICPP patients are closely related to carbohydrate metabolism, hyperandrogenism, and insulin resistance, indicating similar pathogenesis with polycystic ovary syndrome.

关键字 Idiopathic central precocious puberty, gut microbiota, hyperandrogenemia, insulin resistance, polycystic ovary syndrome

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Early-life risk factors for Chinese children with food sensitization: comparative study of surveys in 2009 and 2019

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Background: Many countries have recorded the change of food sensitization (FS) prevalence in the past decade. Little is known about epidemiological trends of childhood FS and its risk factors in China.
Objective: To investigate the change of early-life risk factors associated with childhood FS prevalence over the past decade.
Methods: Two cross-sectional surveys were conducted using the same method in 2009 and 2019, all children were recruited in summers. All participate underwent skin prick test and took medical histories. Meanwhile, their parents/guardians completed a single-choice questionnaire about relevant early-life environment exposures, including demographic characteristics, feeding patterns, delivery way and siblings or pets. The prevalence of FS was compared by Chi-square test. Logistic regression was performed to obtain the odds ratios (OR) of factors contribution to FS.
Results: The prevalence of FS was 18.0% (72/401) in 2009 and was 15.6% (80/513) in 2019, there was no significant statistical difference (P=0.342). In the 2009 survey, older age [aOR1.07, 95% CI (1.02-1.13)] and children with a family history of allergic disease [aOR2.01, 95% CI (1.12-3.61)] increased the risk of FS, but formula-feeding before 4 months old compared with breast-feeding did not increase the FS prevalence. In the 2019 survey, the effect of age [aOR1.04, 95% CI (1.00-1.09)] and formula-feeding [aOR0.42, 95% CI (0.21-0.83)]on the prevalence of FS did not change, while family history was no longer a risk factor. Male [aOR1.67, 95% CI (1.03-2.81)] was an added risk factor of increase the FS prevalence.
Conclusion: The FS prevalence has stabilized in Chongqing, China since 2009. The effect of family history on FS seems to be diminishing. Formula-feeding in the first 4 months of life compared with breast-feeding did not increase the risk of FS.

关键字 Keywords: Food sensitization; Prevalence; Risk factor; Family history; Children

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Prevalence of malnutrition and associated factors in children aged 6－24 monthsunder poverty alleviation policy in Shanxi province, China

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Background: The nutrition improvement project of children in poverty-stricken area, which is co-carried out by China National Health. This project implemented the central finance to apply free nutritious food Ying Yang Bao (YYB) to 6-24 months old infants, in order to prevent infant malnutrition and improve the level of children health in poor regions. **Methodology:** A total of 3431 IYC were studied with a set of questionnaires from the 10th September 2020 to 31th October 2020 in the province of Shaanxi, China, dividing it into three regions including Northern of Shaanxi, Northern of Shaanxi and Guan Zhong. Parents for IYC aged 6-month-old, 1,125 for aged 12-months-old and 1,167 for aged 18 to 24-months-old were interviewed. A cross-sectional study was conducted. Both Univariate Analysis and Multivariate Logistic Regression Analysis were performed. **Result:** The stunting rate of IYC in northern of Shaanxi province was less than 5%, however, the proportion of overweight was more than 14%.the incidence of dysplasia in Guan Zhong is less than 1%, the rate of overweight was less than 7%. The stunted growth rate in Northern of Shaanxi is higher than that of the other two regions. (P<0.01), The low weight rate in the three regions accounted for less than 0.5%; The wasting rate of the three regions was between 1% and 2%. Prevalence of stunting in IYC aged 6~month-age group is more than other two groups (P<0.05). The proportion of overweight in three-month-age stages in Shaanxi respectively was 8.96%,8.71%,7.80%, there is no significant difference in three month-age groups(P>0.05).Univariate analyses revealed that Children who had premature birth and Prevalence of malnutrition among Children under 24 Months were more malnutrition(p<0.05). Normal birth weight Children who had malnutrition (29.6%) was less than underweight IYC, but no statistical difference (p>0.05), children with breastfeeding were less likely to have malnutrition, but no statistical difference(p>0.05). However, as parity increases, proportion of malnutrition decreases, the difference has very obvious statistical significance (p<0.01). In addition, higher the education level of children’s parents, higher family income, caregivers having more health education knowledge, the lower the prevalence of children malnutrition (p<0.01), meanwhile, children who took YYB and other nutrients, the prevalence of malnutrition also declined(p<0.05).Multivariate model showed that Compared with children in different areas, children in Northern of Shaanxi were at more increased risk of malnutrition than other two regions (OR=2.24; 95% CI: 1.68－2.98). Children in the18－24 months age group were more malnutrition than children in other groups (OR=0.746; 95% CI: 0.61－0.91). In addition, we found that children in lower education degree of parents (OR=0.79; 95% CI: 0.66－0.95), were at higher risk of malnutrition compared with children in higher education degree group. IYC had a higher prevalence of malnutrition on parity more than 3(OR=1.52; 95% CI:1.10－2.10) compared with those parity less than 2. Make supplementary food separately was associated with decreased risk of malnutrition (OR=0.79; 95% CI:0.66－0.95). Besides, the association of children taking YYB, iron supplementation and other nutrients was significant (OR= 0.77; 95% CI:0.65－0.90). Correct supplement food time was also very

important (OR= 0.85; 95% CI: 0.71－1.00).**Conclusion:** the prevalence of stunting, underweight, wasting was reduced greatly, relatively low, however the rate of overweight increase was relatively large. Our findings revealed that additional risk factors for malnutrition included guardian not making supplementary food separately, not adding supplementary food at the right time, not taking the distributed YYB for IYC etc. It is necessary to strengthen the dissemination of nutrition and health education. Dietary structure analyses explain the underlying causes of malnutrition and improvement in further study.

关键字 Prevalence of malnutrition; Associated factors; Poverty alleviation policy

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SIRT1 mediates growth hormone resistance through JAK2/STAT5 signaling under caloric restriction conditions

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Objective: Growth hormone (GH) is critical to children's growth and development, and it plays its biological role mainly through IGF-1. GH/IGF-1 signaling in the liver is regulated by the nutritional status of the body.SIRT1,a ptotein deacetylase,plays an essential role in adative metabolic and endocrine responses.The purpose of the present study was to investigate the regulatory effect of SIRT1 on GH/IGF-1 signals in livers and its potential mechanisms under caloric restriction .Methods: The expression of SIRT1 were investigated in the liver of mice under caloric restriction conditions.Next, the effect of SIRT1 on GH/IGF-1 axis in the liver of mice under caloric restriction conditions.Finally,the key protein expression level of JAK2/STAT5 in GH signal under caloric restriction conditions. Results: The expression levels of SIRT1 in liver was up-regulated under caloric restriction ,and SIRT1 negatively regulated the production of GH-dependent IGF-1 in the liver,further studies found that SIRT1 negatively regulated the phosphorylation level of GH-dependent STAT5.
Conclusion: SIRT1 regulates GH/IGF-1 signaling in the liver by altering STAT5 activity , which leading to GH resistance under caloric restriction .This study will provide new insights into the mechanisms of GH resistance under caloric restriction.

关键字 Growth Hormone Resistance, SIRT1, STAT5,Caloric Restriction.

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Comparison of Fecal Calprotectin levels and Growth Status between infants with milk protein allergy and healthy infants

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Background: Food allergy in children is a serious and often life-threatening health issue affecting approximately 4% of children and their families worldwide. In the early stage, our research group investigated and evaluated the normal levels of fecal calprotectin in healthy children aged 0-4 . In this study, the purpose was to compare the fecal calprotectin level and growth status of infants with or without milk protein allergy, to prove that the fecal calprotectin of infants with milk protein allergy increased and the high concentration of fecal calprotectin have an adverse effect on the growth and development of infants.
Methods: The study was conducted at the Department of Developmental and Behavioral Pediatric and Child Healthcare. According to the criteria for the diagnosis of food allergy, infants who meet the diagnostic criteria are included in the allergic group, and those who do not meet the diagnostic criteria are included in the control group. Infants under 1 year old, especially infants within 3 months of age, have higher fecal calprotectin levels and show greater individual differences. So, in order to reduce the difference and improve the accuracy of the research, this study divided the subjects into three age groups, 0~3 months, 3~6 months (not including 3months) and 6~9 months (not including 6months), according to the age at the time of consultation. Stool samples were collected and analysed, and the fecal calprotectin concentration was determined via an enzyme-linked immunosorbent assay. Infants' weights and lengths were measured. The parents completed a brief questionnaire with questions about several clinical andsociodemographic factors.
Results: The study enrolled 180 subjects - 90 milk allergy infants (41 boys, 49 girls) and 90 healthy infants (51 boys, 39 girls). The median fecal calprotectin level calculated for all 90 infants in the allergic group was 410 μg/g faeces (interquartile range: 168-1739 μg/g). The median fecal calprotectin level calculated for all 90 infants in the control group was 141 μg/g faeces (interquartile range: 41-373 μg/g). Compared with that in the control group, the fecal calprotectin level in the allergic group was significantly higher z=-9.335, $p<0.001$). At 0~3 months of age, the median fecal calprotectin level in the allergic group was 514 μg/g (interquartile range: 202~1760 μg/g), and the median fecal calprotectin level in the control group was 217 μg/g (interquartile range: 54~766 μg/g). Compared with that in the control group, the fecal calprotectin level in the allergic group was significantly higher (z=-3.676, $p<0.001$). At 3~6 months of age, the median fecal calprotectin level in the allergic group was 330 μg/g (interquartile range: 171~1753 μg/g), and the median fecal calprotectin level in the control group was 143 μg/g (interquartile range: 40~297 μg/g). The fecal calprotectin level in the allergic group was significantly higher than that in the control group (z=-6.768, $p<0.001$). At 6~9 months of age, the fecal calprotectin level was significantly higher in the allergic group (median: 426 μg/g; interquartile range: 126~1773 μg/g) than in the control group (median: 110 μg/g; interquartile range: 13~171 μg/g; z=-5.525, $p<0.001$). The LAZ, WAZ and WLZ in the allergic group were significantly lower than those in the control group (t=-2.250, $p=0.026$; t=-4.178, $p<0.001$; t=-3.229, $p=0.001$, respectively).

Conclusion: The fecal calprotectin level in the milk protein-allergic group was significantly higher than that in the healthy group. And the high concentration of fecal calprotectin have an adverse effect on the growth and development of infants.

关键字 Fecal calprotectin; Milk protein allergy; Growth

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Can fecal calprotectin levels be used to monitor infant milk protein allergies?

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Background: Food allergies have a serious impact on the physical and mental health of children, affecting their growth and development and reducing their quality of life and learning. More than 10% of infants under the age of 1 have been shown to have allergic reactions to at least one common allergenic food, and a milk protein allergy is one of the most common food allergies, with an incidence of 2-3%. Food allergies are often considered the first step in the process of allergies. With age, food allergies are more likely to cause serious allergic diseases, such as asthma. Therefore, early diagnosis of and intervention for food allergies in infants and young children will help prevent the further development of allergic diseases, but there are no early predictive indicators for monitoring infant food allergies. A milk protein allergy in infants' gastrointestinal (GI) symptoms are more common and severe. Fecal inflammatory biomarkers, such as calprotectin in infants with an allergy to cow's milk protein, have been taken into consideration. The detection of fecal calprotectin adopts enzyme-linked immunosorbent assay, which is fast, simple and reproducible and thus it can be used as a noninvasive, inexpensive, simple and sensitive marker of intestinal inflammation. In our previous study, fecal calprotectin, as an inflammatory factor, was shown to possibly play an important role in food allergy detection. We aimed to test whether fecal calprotectin can be used to monitor food allergies in infants by comparing the fecal calprotectin levels in infants with a milk protein allergy before and after an intervention treatment.
Methods: This study was performed at the Department of Developmental and BehavioralPediatric and Child Healthcare of Xinhua Hospital affiliated with Shanghai Jiao Tong University School of Medicine. Infants with allergies and healthy controls were enrolled. Infants diagnosed with milk protein allergy received dietary intervention (involving amino acid formula or deep hydrolysis formula or mothers avoiding milk, eggs and other allergic foods), and the allergy group was followed up one month and two months after the intervention. Stool samples were collected at follow-up, and the concentration of fecal calprotectin was determined using enzyme-linked immunosorbent assay. The infant's weight and length were measured.
Results: The allergic group comprised 90 milk-allergic infants (41 boys, 49 girls), and the control group comprised 90 healthy infants (51 boys, 39 girls). Compared with the fecal calprotectin level in the control group (141 μg/g), that in the allergic group (410 μg/g) was significantly higher ($z=-9.335$, $p<0.001$). After two dietary interventions and treatments, the fecal calprotectin levels of the infants with a milk protein allergy at the first (253 μg/g) and second follow-up visits (160 μg/g) were decreased significantly compared with those before the intervention ($z=-7.884$, $p<0.001$ and $z=-8.239$, $p<0.001$, respectively). The growth index values (LAZ and WAZ) of the infants with a milk protein allergy at the first follow-up visit and at the second follow-up visit were significantly higher than those before dietary intervention ($p<0.05$). Fecal calprotectin was negatively and significantly correlated with the WLZ and WAZ at the second follow-up visit (Spearman's rho=-0.234, $p=0.01$ and Spearman's rho=-0.193, $p=0.03$, respectively).
Conclusion: The level of fecal calprotectin in infants with a milk protein allergy decreased after a dietary intervention. The level of fecal calprotectin may be used

to monitor the improvement of intestinal allergies in infants with a milk allergy and may be used as a possible biological indicator for follow-up and monitoring of intestinal allergies.

关键字 Fecal calprotectin; Milk protein allergy; Intervention: Follow-up; Monitoring

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The Protective Effect and Potential Mechanism of NRXN1 on Learning and Memory in ADHD Rat Models

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The learning and memory network is highly complex and remains unclear. The hippocampus is the location of learning and memory function. Impairment of synaptic morphology and synaptic plasticity (i.e., long-term potentiation) appears to cause learning and memory deficits. Several studies have indicated the role of NRXN1 in regulating the synaptic function, but little is known on its role in learning and memory dysfunction associated with attention deficit and hyperactivity disorder (ADHD). Our results showed that overexpression and interference of NRXN1 in vivo, respectively, affected learning and memory, as was assessed by Morris water maze tests, in spontaneously hypertensive rats (SHRs) and Sprague Dawley (SD) rats. We found that SD rats performed better after methylphenidate (MPH) treatment in salvage trials. Accordingly, the change of NRXN1 led to altered synapse-related gene (PSD95, SYN1, GAP43, NLGN1) expression, further providing evidence of its role in the maintenance of synaptic plasticity. We also verified that the expression of synapse-related genes synchronously changed with NRXN1expression in the behavioral assessment. The expression of NRXN1 was confirmed to affect the expression of synapse-related genes after its interference and overexpression in the primary hippocampal neurons in vitro. These results confirmed our hypothesis that NRXN1 might nucleate an overall trans-synaptic signaling network that controls synaptic plasticity and is responsible for impairments in learning and memory in ADHD. These findings suggest a possible protective role of NRXN1 in learning and memory in ADHD. Further RNA-seq sequencing revealed significant differences in the expression of 5-hydroxytryptamine receptor (5-HT6R), which was further verified at the cellular level, and the mechanism of NRXN1 affecting synaptic plasticity was preliminarily discussed.

关键字 NRXN1; learning and memory; synaptic plasticity; hippocampus; SHR; ADHD; 5-HT6R

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The Clinical Curative Effect of 5 Kinds of Intervention Methods on Children with Diarrhea: A Network Meta-Analysis

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Abstract: Objective: To evaluate and compare the effects of various intervention methods used to shorten the duration of diarrhea in children with diarrhea. Methods: The published literature that correlated with different interventions in children with diarrhea in Cochrane Library, EMbase, Springerlink, Elsevier, Pubmed, Medline, CNKI, CBM, VIP and Wanfang medical databases were collected. The search time limit has been from the establishment of the database to the present (June 2021).With formulated inclusion and exclusion criteria, the literature was screened, and the information was extracted. The network relationship between the studies was showed through STATA 15.0, and the area under the cumulative ranking probability graph showed the possibility of each intervention method becoming the best intervention. Results: An amount of 31 available documents referring to 3,346 children with diarrhea, and we have found that montmorillonite powder has the best effect on shortening the duration of diarrhea in children, followed by Bifidobacterium and massage. Conclusion: Montmorillonite powder has significant effects in shortening the length of diarrhea in children with diarrhea, and can provide reference for clinical practice.

关键字 Keywords: children; diarrhea; network meta-analysis

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Positive effects of oral motor intervention on neurobehavioral development in preterm infants: a clinically randomized controlled study

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Objective:To evaluate the effect of oral motor intervention on neurobehavior of premature infants, and to establish an intervention model of oral exercise on neurobehavior of premature infants.
Methods:84 cases of premature infants were collected from June 2020 to December 2020.84 patients were randomly divided into intervention group and control group, 42 in each group. The intervention group received oral exercise intervention (oral stimulation and non nutritive sucking), and the control group received routine nursing. The self-made basic data recording form was used to collect the body weight, milk volume, oral motor ability before intervention, 7 days and 14 days after intervention, and the neurobehavioral scores before and 14 days after intervention, as well as the information of intelligence development index and psychomotor development index corrected at 3 months of gestational age. The general data of the two groups were analyzed by SPSS;Neurobehavioral score, body weight, milk volume, oral motor ability, MDI and PDI were tested by two independent samples t test.
Results:(1)There was no significant difference in gender, gestational age,birth weight, Apgar score, twins or multiple, prenatal fetal heart rate, fetal movement, preterm birth causes between the two groups ($P > 0.05$).(2)There was no significant difference in age, education level, mode of pregnancy and mode of delivery between the two groups($P > 0.05$).(3)The NBNA score of the intervention group was higher than that of the control group on the 14th day after OMI;after the intervention, the number of qualified preterm infants in the two groups increased, and the abnormal rate gradually decreased, with significant difference between the two groups ($P < 0.05$).(4) The average value of MDI and PDI in the intervention group was higher than that in the control group. The levels of MDI and PDI in the two groups were in the middle level, and the difference was statistically significant ($P < 0.05$).(5) The oral motor ability of premature infants in the two groups was compared, and the difference between the two groups was statistically significant on the 14th day after intervention ($P < 0.05$).The score of premature infants at different time points was statistically significant ($P < 0.05$),and there was interaction between group and time in the two groups.
Conclusion:(1)Oral exercise intervention can effectively improve the neurobehavioral ability of preterm infants, improve the passing rate of NBNA score of preterm infants, and the intervention is simple and safe, which can be used to improve the behavioral development and prognosis of preterm infants.(2) Oral motor intervention in hospital can promote the establishment of oral feeding ability of premature infants, which is achieved by accelerating neural development.

关键字 神经行为；早产儿；口腔运动；智力发育

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MicroRNA-506 modulates insulin resistance in human adipocytes by targeting S6K1 and altering the IRS1/PI3K/AKT insulin signaling pathway

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Abstract
The incidence of obesity has increased rapidly, becoming a worldwide public health issue that involves insulin resistance. A growing number of recent studies have demonstrated that microRNAs play a significant role in controlling the insulin signaling network. For example, miR-506-3p expression has been demonstrated to correlate with insulin sensitivity; however, the underlying mechanism remains unknown. In this study, we found that miR-506-3p enhanced glucose uptake by 2-deoxy-D-glucose uptake assays and regulated the protein expression of key genes involved in the PI3K/AKT insulin signaling pathway including IRS1, PI3K, AKT, and GlUT4. We next predicted ribosomal protein S6 kinase B1 (S6K1) to be a candidate target of miR-506-3p by bioinformatics analysis and confirmed using dual-luciferase assays that miR-506-3p regulated S6K1 expression by binding to its 3′ -UTR. Moreover, modulating S6K1 expression counteracted the effects of miR-506-3p on glucose uptake and PI3K/AKT pathway activation. In conclusion, miR-506-3p altered IR in adipocytes by regulating S6K1-mediated PI3K/AKT pathway activation. Taken together, these findings provide novel insights and potential targets for IR therapy.

关键字 miR-506-3p; S6K1; IRS-1/PI3K/AKT signaling pathway; insulin resistance, obesity

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Influence of Asthma on Sleep Quality in Preschool Children

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Background: Many studies have reported that asthma was associated with poor sleep quality in school-aged children. However, research on asthma-related sleep problems in preschool children has been limited. Our study aimed to explore the effect of asthma on sleep quality in preschool children, by using a comprehensive sleep questionnaire.
Methods: 268 children aged from 4-7 years old were recruited randomly from 5 kindergartens in Taizhou, Zhejiang Province, China. The information on physician-diagnosed asthma and asthma-related demographic data were collected by questionnaires. The sleep quality was assessed using the Children’s Sleep Habits Questionnaire (CSHQ). A higher CSHQ score indicated more sleep problems, and a global CSHQ score > 41 was identified as poor sleep quality.
Results: The prevalence of asthma was 5.7%. Sleep scores were higher in the children with asthma compared with those without asthma on total sleep quality (ß =7.2, 95% CI= 0.2, 14.2, p <0.05), as well as the night wakings subscale (ß =1.0, 95% CI= 0.1, 1.9, p <0.05) and the sleep disordered breathing subscale (ß =0.8, 95% CI= 0.0, 1.5, p <0.05) after adjusting for confounders. Children with asthma were significantly more likely to have poor sleep quality than non-asthmatic children (OR=20.3, 95% CI= 1.8, 230.4, p<0.05). In addition, asthmatic children had a significantly higher risk of sleep disordered breathing compared with those without asthma (OR=7.7, 95% CI= 1.0, 57.4, p<0.05).
Conclusions: Asthma has an adverse impact on preschool children's sleep quality, especially in the subscales of night wakings and sleep disordered breathing.

关键字 asthma，sleep quality，CSHQ，preschool children

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Altered metabolic profile in plasma of young boys with autism spectrum disorder

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Background: Autism Spectrum Disorder (ASD) is a serious neurodevelopmental disorder with no clinical biomarker. In this study, we aim to discover metabolic features in plasma that can discriminate children with ASD from typically developing (TD) children and explore the relationship between metabolites and developmental abnormalities in ASD children.
Methods: The study included 29 boys with ASD (age: 3.02±0.67 years) and 30 matched TD children (age: 3.13±0.46 years). Autism Behavior Checklist (ABC), Childhood Autism Rating Scale (CARS) and Gesell Developmental Schedules (Gesell) were used for developmental and behavioral assessments of ASD children. Plasma samples of all the participants were analyzed by liquid chromatography-tandem mass spectrometry (LC-MS/MS). Both multivariate and univariate analysis were applied to search for differential metabolites between ASD and TD group. To further identify biomarkers for ASD cases, linear Fisher Discriminant Analysis (FDA) and Receiver Operating Characteristic (ROC) analysis were conducted. The association between metabolite concentration and scale score was assessed using Spearman rank correlation.
Results: A total of 645 metabolites were present at different concentrations in the two groups, among which 14 metabolites have annotation in KEGG pathway. The arachidonic acid metabolism was significantly upregulated in ASD children. In ROC analysis, we identified 3 indicators (ornithine, 3-butynoate, and arachidonic acid) that could discriminate between ASD and TD group. For the three indicators, ornithine had the highest AUC (Area under ROC) value. Furthermore, the concentration of choline, ornithine, benzoic acid and prostaglandin d2 was found to be correlated with ABC scores in ASD children.
Conclusions: Children with ASD showed different metabolic patterns, especially in the upregulation of arachidonic acid metabolism. Ornithine may have the potential to be the biomarker of ASD children. The levels of metabolites were related to developmental abnormalities in ASD children.

关键字 Autism Spectrum Disorder (ASD), plasma, liquid chromatography-tandem mass spectrometry (LC-MS/MS), metabolic profile

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Exercise Training combined with Mindfulness Therapy for Attention-deficit hyperactivity disorder in Three children

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[Background]
Attention-deficit hyperactivity disorder (ADHD) is a common psychiatric disease in children and adolescents. This children often fail to complete learning tasks due to difficulty in continuous concentration of attention, uncontrollable hyperactivity and control emotions. In addition, there are also certain damages in social communication and executive function. Prospective longitudinal studies have shown that as age increases, the core symptoms of ADHD will decrease, but social function deficits still persist. Therefore, early intervention for ADHD children is essential. At this stage, the treatment of ADHD includes drug and non-drug therapy.There are many non-drug treatments for children with ADHD, including emotional training, exercise training, cognitive training, social training and so on. Most guidelines recommend starting with non-drug therapy and adopting a gradual treatment method, but the effectiveness has not been fully confirmed.However, there is no report on the Exercise Training combined with Mindfulness Therapy in the treatment.

There are few reports on the application of exercise training in children with ADHD in domestic literature, and the form of exercise is single. A foreign Meta-analysis discussed the use of exercise training in children with ADHD. The results show that aerobic exercise can improve cognitive, and they can make children easier control emotion and improve physiological indicators.Our therapy is a systematic method and it is easier to be extended to other ADHD children. This paper groundbreakingly reports the efficacy of Exercise Training combined with Mindfulness Therapy in three children, so as to the clinical treatment of ADHD children.

[Method]
The contents of exercise training are as follows in chronological order: basic exercise, endurance exercise, coordinated exercise and controlled exercise. The Mindfulness training content is that guide the child focus on himself. The training duration starts from 10 minutes and the maximum time is 20 minutes. In addition, the cognitive training, mainly visual training, is supplemented. We draw graphics on the scatter chart and let the children copy and the difficulty increases gradually with the process of time. Exercise Training combined with Mindfulness Therapy lasts 20 weeks. Before and after the intervention, the patients were evaluated by the SNAP-IV scale to evaluate the symptoms and severity of the children, and the Parent Symptom Questionnaire (PSQ) was used. The Weiss Functional Impairment Scale-Parent form (WFIRS-P) assesses functional deficits.

[Results]
According to the results of SNAP-IV, three cases have different symptom types. Case 1 had abnormal scores in opposition, attention deficit and hyperactivity-impulsiveness before training, and the scores of the three items

decreased to normal after training. Case 2 had abnormal scores of opposition before. After training, it is marginal. Before and after training, attention deficit score is marginal. In Case 3, the score of attention deficit items was abnormal before training and decreased to normal after training. According to the results of WFIRS-P, the functional impairment items of Case 1 and Case 2 reduced, and the items of Case 3 were the same as before. It can be seen that according to this scale, this therapy is effective in Case 1 and Case 2. The results of PSQ showed that and most of scores decreased or remained unchanged, only the scores in Case 2 factor 3 increased slightly, which maybe due to fluctuations. The overall score showed a downward trend. According to the results of PSQ, the therapy was generally effective.

[Conclusions]
Based on the children performance and scale evaluation results, Exercise Training combined with Mindfulness Therapy is effective in three children with different symptom types of ADHD. As a new treatment method, there is no relevant researches at home and abroad. This paper hopes to provide a new idea for the non-drug therapy of ADHD.

关键字 ADHD; Exercise training; Mindfulness

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The Effectiveness and Safety of HuiZhiSu in Children with Attention-deficit hyperactivity disorder

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[Background] Attention-deficit hyperactivity disorder (ADHD) is a common developmental disorder during childhood, with an average prevalence of 5.29%. The symptoms are mainly attention deficit, hyperactivity disorder and impulsive personality. Meanwhile, it will suffer from other mental disorders and psychosocial problems, resulting in functional damage in school, work, social communication and so on. At present, ADHD needs long-term treatment. Stimulants are the first consideration, but the treatment rate is less than 20%, and there are many side effects. According to relevant researches on intestinal flora, healthy diet has a protective effect on ADHD, on the contrary, deeply processed desserts, pigments and food additives can increase the morbidity to ADHD. The intake of grains, meat, beans and fruits can improve ADHD symptoms significantly. However, there is still short of scientific clinical data. Therefore, it is imperative to carry out natural therapy that based on improving nutrition. HuiZhiSu is an active ingredient that extracted from rice bran, soybean and angelica dahurica by nanotechnology. As a functional food in clinical, it can be used in adjuvant treatment of developmental problems of children. Whether it can Improve symptoms of ADHD still need scientifically observe and test. The main purpose of this study was to evaluate the efficacy and safety of Huizhisu in the treatment of Attention-deficit hyperactivity disorder (ADHD) children.

[Method] This was a multi-center and clinical observation, 52 children (aged 6-13 years, 8.73±2.069 years; 42 males, 10 females) would complete an 8-week visit. They would use HuiZhiSu to improve their condition without other drugs during the visit. Doses raged as follows: age<12 years old, the dose is 3g/day (1.5g /package), take it twice; age>12 years old, 6g/day, take it twice, in morning and evening. We use ADHDRS-Ⅳ-Parent: Inv and Clinical General Impression Rating Scale (CGI) to evaluate and compare the efficacy in the baseline, 2 weeks and 8 weeks of treatment. At the same time, the efficacy and safety were assessed with vital signs, physical examination, laboratory and ECG examination and adverse event evaluation at the baseline and 8 weeks.

[Results] According to the measurement of ADHDRS-Ⅳ-Parent: Inv, the total score, inattentive and hyperactive/Impulsive subscale score of 52 samples were significantly lower than baseline (t=9.629, p<0.001; t=10.652, p<0.001; t=6.580, p<0.001). After 8 weeks, the score were lower than 2 weeks (t=5.590, p<0.001; t=4.689, p<0.001; t=4.905, p<0.001). Significant improvement in CGI was also observed. The scores at baseline, 2 weeks and 8 weeks were 4.55±0.783,

4.10±0.774, 3.33±0.653, respectively. The data showed that the severity decreased at 2 weeks of treatment ($t=5.814$, $p<0.001$). Compared with 2 weeks, 8 weeks of treatment, the severity was decreased significantly ($t=6.934$, $p<0.001$). After 8 weeks of treatment, there were no seriously ill children, and one child score was evaluated as normal range. The overall progress reflected that 71.2% of the cases had progress at 2 weeks and 92.2% at 8 weeks. HuiZhiSu has high safety, at the same time, there is no clinically significant physical signs and laboratory changes found in 52 samples, and no adverse reactions were reported.

[Conclusions] In this open-label experiment, HuiZhiSu as a functional food is available in improve symptoms of ADHD children, with high safety and no other side effects. HuiZhiSu can be another choice for children with ADHD potentially. But, it still need a double-blind controlled study in the follow-up time.

关键字 ADHD; HuiZhiSu; Food therapy; open-label experiment

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Impacts of vitamin D on emotion and behavior in children and mechanism mediated by gut brain axis

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【Objective】
The prevalence of emotional and behavioral problems among preschoolers (aged 3-6 years) in China is as high as 48.2%. Epidemiological studies suggest that vitamin D (VitD) is related to emotional behavior problems, which are closely related to the influence of microorganisms on brain function through gut brain axis. However, there is no definite research on how VitD affects children's emotional behavior through the mechanism mediated by intestinal flora.
【Methods】
(1) A total of 400 preschoolers between the ages of 3 and 6 in three kindergartens in Shanghai were enrolled. The concentrations of serum 25(OH)D were measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS), and the evaluation of preschoolers' emotion, behavior and attention was obtained by standardized questionnaire.
(2) We established different 25(OH)D levels of immature mice models by feeding different doses of VitD3 after birth, including VitD deficiency group (VDD, 25 IU/kg), VitD overdose group (VDO, 8000 IU/kg) and control group (CTRL, 400 IU/kg), as well as two intervention groups: supplement group (VDDR) and recovery group (VDOR). The behavioral phenotypes of emotion, cognition and attention were detected by standard behavioral paradigm. By c-Fos immunofluorescence staining, the activity of neurons affected by VitD was determined, and the possible key brain areas were screened.
(3) The composition of intestinal flora and the concentration of intestinal SCFAs were detected by 16s rDNA sequencing and LC-MS/MS, respectively. The enzyme activity of cAMP-PKA-pCREB pathway and the expression of downstream genes in prefrontal cortex (PFC) were measured by RT-PCR、Western Blot and ELISA. The serum concentrations of SCFAs and neurotransmitters related with emotion and behavior were determined by LC-MS/MS.
【Results】
(1) There was a U-shaped relationship between serum 25(OH)D and the emotional, behavioral, and attentional power levels of scales in preschoolers. Compared with the group of median 25(OH)D level (20~40 ng/mL), the risk of inattention, impulsive hyperactivity, emotional and behavioral problems increased in <20 ng/mL group and in >40 ng/mL group.
(2) Compared with the CTRL group, the spontaneous activity and anxiety level of VDD and VDO mice were increased. Meanwhile, the behavior of VDD group was more aggressive, with impaired spatial memory and sustained attention.
(3) At baseline, VitD deficiency or overdose could increase the activation of neurons in PFC.
(4) VitD affected the composition and abundance of intestinal flora including Bifidobacterium. Meanwhile, metabonomic targeted analysis showed that VitD influenced the intestinal concentration of SCFAs, especially propionic acid.
(5) The concentration of SCFAs in intestinal tract was positively correlated with the concentration of SCFAs in serum. Compared with CTRL group, the serum concentrations of DA and 5-HT were significantly altered in VDD and VDO group. And the serum DA was negatively correlated with serum propionic acid.

(6) The expression of TH gene in PFC of VDD mice were significantly decreased, the activity of AC and the concentrations of cAMP and PKA were decreased. The expression of the BDNF gene decreased significantly in PFC in VDO mice.
【Conclusions】
Either low or high levels of VitD might have adverse effects on preschool ers' emotion, behavior and attention. VitD deficiency/overdose could affect the emotional behavior, cognition, and attention performance of immature mice. The PFC might be the key brain regions of VitD affecting emotion, behavior and attention. VitD influenced the composition and abundance of intestinal flora including Bifidobacterium, as well as intestinal SCFAs.The increase of intestinal propionic acid synthesis caused by VitD deficiency could regulate the expression of TH gene in PFC through downstream cAMP-PKA-pCREB pathway, and further affect the role of neurotransmitter system, e.g., DA.

关键字 Vitamin D; preschoolers; emotional and behavioral problems; animal model; gut brain axis

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Effect of chromosome microarray analysis on clinical management of children with unexplained developmental delay/intellectual disabilities

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Background: The chromosome microarray analysis (CMA) test for copy number variations (CNVs) is now recommended as a first-line test to evaluate individuals with neurodevelopmental disorders, but its application in China is relatively late. The purpose of this study was to evaluate the diagnostic value of CMA in children with Developmental Delay (DD) and Intellectual Disability (ID) in our clinic and to explore the significance of CMA results for clinical management.
Methods: A total of 248 Chinese children with unexplained DD/ID who visited our clinic were analyzed by the Affymetrix® CytoScan™ 750K Array.
Results: A total of 248 unexplained DD/ID children were enrolled, including 164 boys and 84 girls. In 34 children (19 boys and 15 girls), CNVs were detected to be pathogenic or likely pathogenic, with the overall CMA diagnostic yield of 13.7%. The highest diagnostic yield was 35.1% in the group of <2 years old. In 34 patients, 15 (44.1%) were diagnosed with known syndrome (including Smith-Magenis syndrome, Williams-Beuren syndrome, Potocki-Lupski syndrome, et al). Ten repeated variants (n≥2) distributed at 4 chromosomal loci were found. After obtaining definite molecular diagnosis, the 15 children (44.1%) underwent further clinical examinations and were referred to corresponding specialties for further treatment. The parents of 24 children (70.6%) sought genetic counseling on the doctor's recommendation.
Conclusions: Our results provide information on genetic variation in DD/ID children in China by CMA. The application of CMA in clinic is beneficial to the early diagnosis and intervention of DD/ID children.

关键字 chromosome microarray analysis, copy number variations, Developmental Delay, Intellectual Disability

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Compositional differences between preterm milk of different gestational ages with the term milk: a comparative lipidomic study by LC-MS/MS

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Background: Studies are beginning to emerge on the important biological effects of the milk lipids exerted on the recipient infant, especially on the premature infants. The aim of this study was to comprehensively describe lipidomic differences between preterm milk of different gestational ages with the term milk over the course of lactation.
Methods: Breast milk samples were collected from 88 mothers giving birth prematurely and 39 mothers delivering at full-term (FT). Lipid profiles were assessed using an LC-MS/MS metabolomics strategy. Orthogonal partial least-squares discriminant analysis (OPLS-DA) and pathway analysis were subsequently performed.
Results: The OPLS-DA score plots significantly distinguished the lipids in preterm milk of different gestation ages from their counterparts in term milk. The concentrations of 10 out of 43 lipid subclasses were found to be persistently higher in preterm compared to term milk over the course of lactation; the diacylglycerol (DAG) and a bioactive subclass fatty acid ester of hydroxyl fatty acid (FAHFA) contributed the most to the differences. In terms of individual lipid species, the ten highest substances found in very preterm (VPT) colostrum compared to FT colostrum mainly come from the phosphatidylethanolamine class and the DAG species. Lipid species from the free fatty acid and FAHFA classes were significantly higher in either extremely preterm (EPT) or VPT mature milk (variable importance in projection > 1, $P<0.0001$ for all). The differential lipids between each preterm group and its term counterpart were predicted to be mainly involved in six metabolic pathways, including glycerophospholipid metabolism, glycosylphosphatidylinositol (GPI)-anchor biosynthesis, linoleic acid metabolism, alpha-Linolenic acid metabolism, arachidonic acid metabolism and glycerolipid metabolism.
Conclusions: The lipids in preterm and term milk showed substantial differences, which may be critical for postnatal growth, as well as the neural and immune development of newborns, especially EPT and VPT.

关键字 human milk; lipidomic; LC-MS/MS; very preterm; extremely preterm; infants

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Effectiveness of an Online-delivered Project ImPACT Program for Children with Autism Spectrum Disorder and Their Parents: A Pilot Waitlist Control Study During the COVID-19 Pandemic in China

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Objective: During the COVID-19 pandemic, face-to-face intervention services for families of children with autism spectrum disorder (ASD) were limited. This study aimed to evaluate the effectiveness of an 8-week, online-delivered Project Improve Parents as Communication Teacher (ImPACT) program for children with ASD and their parents in Shanghai, China.
Methods: A pilot non-randomized study with a waitlist control group was conducted in 90 children with ASD and their parents at the Department of Developmental and Behavioral Pediatrics in Xinhua Hospital between April 15, 2020, and March 19, 2021. Participants were allocated to either the intervention (IG) or the waitlist group (WLG) according to their order of recruitment. Parents in the IG immediately received 8 weeks of the online-delivered Project ImPACT program, and the WLG received the same program with a delay when the IG had completed all sessions. Participants in both groups received treatment as usual during the research period.
Results: The online-delivered Project ImPACT program significantly improved the social communication skills of children with ASD. Furthermore, parent’s involvement in the training program produced a collateral reduction in parenting stress and an increase in perceived competence in the parental role. Parents rated the program highly in terms of curriculum schedule, session content, homework assignments, and therapist feedback.
Conclusions: The 8-week, online-delivered Project ImPACT program is a feasible and effective social skill training program for families of children with ASD in China during the COVID-19 pandemic. Future randomized controlled studies in larger sample sizes will be needed to provide further evidence.

关键字 autism spectrum disorder, parent-mediated intervention, online training, social communication, parenting stress

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The Clinical and Experimental Study on Acupuncture for Children with Cerebral Palsy

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Introduction Objective: To investigate the effect of and Acupuncture on brain plasticity and motor development in children with cerebral palsy. Two:To evaluate the effect and mechanism of acupuncture on cerebral palsy.Three:The nerve repair effect of acupuncture on cerebral palsy.
Methods:In this study, 146 cases of brain injury and 1078 cases of cerebral palsy were included by randomized controlled study with ICF (GMFM, Peabody fine motor function, Gesell, muscle tension, joint activity, ADL, TCD, skull B ultrasound, head CT / MRI, SPECT, DTI) evaluation method.
Results:One: the recovery rate of extracellular space (92.3%) was significantly higher than that of the control group (70.8%) (P <0.05), TCD total efficiency (79.3%) was significantly higher than that in the control group (51.8%) (P <0.05). acupuncture to promoting the development of neurological and cognitive movement under 6 months children, effectively reduce the neurological sequelae.
Two: The total effective rate of the children with cerebral palsy was 87% in the acupuncture group, which was significantly higher than that of the control group (P <0.01). The total effective rate of CT / MRI was 59.55% in the acupuncture group and 13.25% higher than that in the control group (P <0.01). The total effective rate was 91.3% in the 1 year follow-up group, which was significantly higher than that in the control group (P <0.01). the FA value of white matter fiber bundle was significantly higher than that of acupuncture at 60 times (P <0.05). The recovery rate of ultrasonous brain injury (86.7%) in acupuncture group was significantly higher than that in control group (64.4%) (P <0.05). The recovery rate of SPECT in acupuncture group was 96.4%, which was significantly higher than that in the control group (P <0.01).
Conclusion: Acupuncture rehabilitation not only promote the development of white matter and gray matter in children with cerebral palsy, but also promote the brain function of children with cerebral palsy remodeling and compensation, and promote social adaptation, language and other cognitive function development, children with cerebral palsy movement and Fine motor function development and recovery, improve the children's self-care ability.
Key Words: Cerebral palsy;Acupuncture;Nerve repair;Nerve recombination;Movement and Fine motor function;Cognitive function development

The research is novel, the design is reasonable, the data is complete, the statistics are correct and the conclusion is credible. Has published 28 papers, including SCI included 3, published monograph 2, invention patents 3, the technology has been incorporated into the Chinese cerebral palsy rehabilitation guidelines (2015). Has a high clinical value and promote the use of value. The evaluation of acupuncture and moxibustion therapy and prevention of cerebral palsy children was not evaluated by ICF comprehensive evaluation system at home and abroad.
Project leader after more than 30 years of clinical exploration and research, improve the cerebral palsy acupuncture massage rehabilitation technology, nearly 7 years in the Guangzhou University of Chinese Medicine Affiliated Nanhai Obstetrics and Gynecology Children's Hospital treatment of children with cerebral palsy 2236

cases achieved good results, and extended to Germany, the United States, Australia, the United Arab Emirates, Russia, Indonesia, Sri Lanka, Malaysia, Hong Kong of China, Macao, Taiwan of China and more than 30 provinces and cities nationwide, a total of 9408 cases of cerebral palsy treatment, the average effective rate of 85.25%, access to significant social benefits. The acupuncture rehabilitation technology to lead and promote the international pediatric cerebral palsy rehabilitation medicine development, reached the international leading level.

关键字 Cerebral palsy;Acupuncture;Nerve repair;Nerve recombination;Movement and Fine motor function;Cognitive function development

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Acupuncture for autism spectrum disorders

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Abstract Autism spectrum disorders (ASD), a severe and pervasive heterogeneous neurodevelopment disorder, is characterized by impaired social interaction and communication, repetitive behavioral patterns, and restricted interests. Many aspects of ASD are still debatable, with elusive and complex etiologies, and no effective therapy exists. At present, many studies have verified the effectiveness and safety of acupuncture in the treatment of autism. However, the results should be explained cautiously due to methodological weakness. In order to obtain powerful evidence of the effectiveness and safety of acupuncture in the treatment of ASD, it is worth designing a study with higher methodological quality. We summarize the potential mechanism of acupuncture in the treatment of ASD. We found the mechanism of acupuncture treatment of ASD is still unclear. On the one hand, due to the complex etiology and biochemical changes of ASD, it is a neurodevelopmental disorder syndrome with a variety of biological factors. On the other hand, there are few basic researches on the mechanism of acupuncture in the treatment of ASD. There is still a long way to go to reveal the secret of this mechanism. Acupuncture has a short history in the treatment of autism, but the application of scalp points has achieved remarkable curative effect. There are different kinds of scalp acupuncture therapy in clinic. Thus, we put forward "Xingnao Kaiqiao scalp acupuncture therapy"and bring forth the need for well-designed, rigorous clinical and experimental studies to provide formidable scientific evidence validating the efficacy and safety of acupuncture in the treatment of ASD.

关键字 Acupuncture; Autism spectrum disorders; Xingnao Kaiqiao scalp acupuncture therapy

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Effects of Quality of Life of Autistic Disorder Children

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Abstract: Objective To investigate quality of life in Autistic Disorder children.This study aimed to evaluate the validity of existing QoL questionnaires for use with children with ASD aged 8－12 years. Method 200 autistic children (male: 118, female: 82; 2~4 years old: 80, 5~7 year old: 87, 8~12 years old: 33) and 120 normal children (control group) are brought into this study. Separate path analyses were performed to evaluate models of QOL and Intelligent evaluation. the PedsQL (Pediatric Quality of Life Inventory) as robust measures used with children with neurodevelopmental disorders.Results In the study,The test group had lower scores on the PedsQL4.0 universality Core scale, in comparison with the control group. Behaviour problems had a negative indirect effect on Community adaptation, mental health and school performance. And a lower intelligence-related quality of life for children with autistic disorder and clinically significant autistic symptoms in comparison with children and fewer symptoms.The quality of life of Autistic Disorder group was lower than normal group in the scores of physical functioning were(62.30±25.05),emotional functioning were(53.57±26.69),social functioning were(44.63±27.91)，and school functioning(38.69±30.60).The totals cores of PedsQL were(49.86±23.32),with the difference being significant(90.16±13.32、79.09±19.56、86.39±15.45、82.75±16.03、85.23±14.2，P<0.01).Conclusions Results suggest greater impairment in adaptive functioning and emotional disorders. For high-functioning autism children, potential positive development played significant roles in rehabilitation, to achieve and maintain the best level of intervention.the severity of the disorder and social support Coping strategies were related with Life self-care ability and adaptation, coping with Intelligent obstacle seriously .Physicians are encouraged to evaluate for early treatment in the overall care plan.

关键字 Autistic Disorder; children ;quality of life; PedsQL4.0

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Psychological distress in parents of children with autism spectrum disorder: a cross-sectional survey based on 683 mother-father dyads

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Objective: This study aimed to assess the psychological distress in parents of children with ASD using a large, gender-balanced samples. Prevalence and predictive factors for parental psychological distress were also studied.
Methods: A cross-sectional survey was conducted for parents of children with ASD and 683 mother-father dyads were included in the final analyses.
Results: Mothers of children with ASD had higher stress, anxiety, and depression levels than fathers, but these differences remained significant only for those whose children had severe autistic symptoms. No significant differences were detected for parents of children with mild-to-moderate autistic symptoms. The prevalence of moderate-to-severe anxiety and depression for mothers were 13.8% and 13.1%, respectively. The prevalence of moderate-to-severe anxiety and depression for fathers were 9.9% and 8.0%, respectively. A college or above education was a protective factor against maternal stress, and an only child contributed to paternal stress. Unemployment status was a significant predictor of maternal stress and depression. Child social impairment predicted maternal psychological distress, and stress was a significant predictor of anxiety and depression for both parents.
Conclusions: Mothers of children with severe autistic symptoms experience more psychological distress. Social skill interventions for children and stress management for parents are advised to promote psychological well-being for patents of children with ASD.

关键字 Autism spectrum disorder; Psychological distress; Parents; Severity of symptoms; Social impairment

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Associations of maternal n-3 polyunsaturated fatty acids with telomere length in placenta and cord blood in Chinese population

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Telomeres system plays important roles in fetal development as well as accelerate cellular dysfunction, ageing and disease susceptibility over the lifespan. Few studies have investigated the correlation between maternal polyunsaturated fatty acids (n-3 PUFAs) and telomeres in newborn and after birth and the underlying influential mechanisms are to be clarified. In this study, we assessed the associations of maternal n-3 PUFAs with telomere length (TL) and associated DNA methylation of telomerase reverse transcriptase (TERT) promoter in the cord blood and the placenta. A total of 274 pregnant women and their newborn babies were enrolled in the study. Maternal blood before delivery, and cord blood and placenta during childbirth were collected. Fatty acids in erythrocytes were measured by gas chromatography. TL in the cord blood and placenta calculated by real-time qPCR products. The TERT promoter methylation was analyzed by DNA bisulfite sequencing. Associations of maternal fatty acids with TL were analyzed by univariate and multivariate regression. We found that low concentrations of maternal DPA and total n-3 PUFAs, and some of n-6 PUFAs (GLA, ADA and OA) and high concentrations of LA and high n-6/n-3 PUFA ratio were associated with shortened TL in cord blood cells (estimated difference in univariate analysis -0.37 to -0.47 for extreme quintile compared with middle quintile), and that low concentrations of cord blood DHA were related to shortened cord blood TL. Differently, higher concentrations of either maternal n-3 PUFAs (LNA, C20:3n-3 and DHA) or GLA were associated with shortened TL (estimated difference in univariate analysis -0.36 to -0.45 for higher quintiles compared with middle quintile) in the placenta. Further examination demonstrated that maternal DHA and total n-3 PUFAs had a positive association with the TERT promoter DNA methylation in the cord blood instead of the placenta. These data suggest the different effects of maternal n-3 PUFAs on TL and associated TERT promoter methylation, between the cord blood and the placenta.

关键字 maternal n-3 fatty acids; newborns; telomere length; telomerase reverse transcriptase; DNA methylation.

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Multimodal study on SHANK3 gene defects: From patient to zebrafish model

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Objective
SHANK3 deficiency represents one of the most frequent, monogenic risk factor for autism spectrum disorder (ASD) and *SHANK3* caused ASD presents a unique opportunity to understand the underlying neuropathological mechanisms of ASD. Here we attempt to investigate the genetype-neuromorphometry-clinical characteristics profiles of Chinese children with *SHANK3* deficiency by neuroimaging, neurobehavioral evaluation and zebrafish model.
Methods
Subjects with *SHANK3* deficiency were recruited and conducted from Aug 1, 2014 to Aug 31, 2021 in the division of child health care of Children’s Hospital of Fudan University. Genetic tests, comprehensive clinical and neurobehavioral evaluations, as well as brain imaging were conducted for these subjects. Furthermore, 26 have idiopathic ASD without *SHANK*3 and other common genetic defect, and 32 were typically developing children as controls to analyze the differences in clinical and neuroimaging characteristics. Genetic mutations including chromosomal deletions and point mutations of *SHANK3* were identified or confirmed by MLPA, chromosome microarray, WES or Sanger sequencing methods. Comprehensive clinical and neurodevelopment evaluations were performed by experienced development pediatricians. Differences in quantitative grey matter indices were assessed using voxel-based morphometry (VBM) while in white matter were analyzed with tract-based spatial statistics (TBSS). We constructed a novel *shank3*-deficient (*shank3ab-/-*) zebrafish model through CRISPR/Cas9 editing and conducted comprehensive morphological and neurobehavioral evaluations, including of core ASD-like behaviors, as well as molecular analyses of synaptic proteins expression levels. Furthermore, different VPA doses and treatment durations were examined for effects on zebrafish ASD-like phenotypes.
Results
A total of 33 children with *SHANK3* defects were included. Phenotypically, we described several previously unreported clinical features and manifestations including nostril eversion, sensory stimulus seeking, dental abnormalities, hematological problem and prominent granulation tissue, as well as common features consisting of hypotonia, global developmental delay, and mild dysmorphic features. For the grey matter, VBM analysis revealed decreased gray matter volume in dorsal striatum, amygdala, hippocampus and parahippocampal gyrus ($P < 0.05$, FWE corrected). For the white matter, TBSS results demonstrated decreased FA in multiple tracts mainly with projection fibers and association fibers, including internal capsule, external capsule, cerebral peduncle, sagittal stratum, and etc. ($P < 0.05$, FWE corrected). For the *shank3*-deficient zebrafish model, compared to wild types, *shank3ab-/-* zebrafish exhibited greater developmental mortality, more frequent abnormal tail bending, pervasive developmental delay, impaired social preference, repetitive swimming behaviors, and generally reduced locomotor activity. The expression levels of synaptic proteins were also dramatically reduced in *shank3ab*$^{-/-}$ zebrafish. These ASD-like behaviors were attenuated by low-dose (5 mM) VPA administered from 4 to 8 days post-fertilization and the effects persisted to

adulthood. In addition, the observed underexpression of grm5, was significantly improved in VPA-treated *shank3ab-/-* zebrafish.
Conclusions
For the first time, we systematically analyzed the genotype-neuroimaging phenotype-behavior phenotype of patients with *SHANK3* deficiency, and constructed a homogenous *shank3* knockout zebrafish model to further verify its morphological and behavioral characteristics. Additionally, we constructed a novel *shank3*-deficient zebrafish model and report for the first time that low-dose VPA administered after neural tube closure has lasting beneficial effects on the ASD-like behaviors. These findings provide a promising strategy for SHANK3 clinical development.

关键字 SHANK3, brain imaging, valproic acid, zebrafish model, autism spectrum disorder

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The differences of the parental and self-report of CSHQ in children with ADHD

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Objectives: To compare the differences of reporting Children’s Sleep Habits Questionnaire (CSHQ) between parents and children with Attention deficit hyperactivity disorder (ADHD).
Method: Cluster random sampling and the method of two stage epidemiology were used. 6035 children aged 6-12 years from five elementary schools in Chongqin, China, completed the questionnaires along with their parents and teachers. The first stage is to fill out ADHD Rating Scale of IV by parents to find potential children with ADHD. The second stage includes Vanderbilt ADHD Diagnostic Teacher Rating Scale(VADTRS) filled out by teachers, Vanderbilt ADHD Diagnostic Parent Rating Scale(VADPRS) and family status questionnaires by parents, and CSHQ by both parents and children themselves.
Results: 528 out of 6035 children were positive for the Vanderbilt scale. Significant difference was found in the CSHQ filled out by parents and children in both Vanderbilt positive group and Vanderbilt negative group, the consistency was poor , the Kappa values of the two groups were both less than 0.4. And there are 6 subscales in CSHQ that all indicate significant differences in sleep disorders reported by parents and children, including: bedtime resistance, sleep duration, sleep anxiety, parasomnia, sleep disordered breathing, and daytime sleepiness.
Conclusion: Children with ADHD are more likely to suffer from sleep disorders than normal children. While parents are more inclined to conclude that their children have sleep disorders. Children's sleep status unilaterally reported by parents is incomplete. The differences of the parental and self-report of the questionnaires comes from the parents' uncertainty about part of the sleep state (resistance to fall asleep, time to fall asleep, number of night awakenings, etc.) of school-age children after separation. Therefore, it is recommended that the CSHQ questionnaire for children after bed separation should be filled out by parents and children together.

关键字 Children, parent, ADHD, sleep disorders, self-report.

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Maternal autoimmune diseases and the risk of mental disorders in the offspring during the first four decades of life: a nationwide cohort study in Denmark

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Importance
Maternal immune activation during pregnancy has been associated with increased risks of several mental disorders in offspring, but few studies have assessed the impact of exposure to autoimmune diseases in utero on full spectrum of mental disorders.
Objective
To investigate the association between maternal autoimmune diseases before childbirth and the full spectrum of mental disorders in offspring.
Design
Population-based cohort study.
Setting
Danish national registers.
Participants
A total of 2 254 234 singletons born in Denmark during 1978-2015.
Exposure
Maternal autoimmune disease diagnosed before or during pregnancy.
Main Outcomes and Measures
Mental disorder defined by hospital diagnosis in offspring. Cox regression was used to estimate hazard ratio (HR) and 95% confidence intervals (CI) for mental disorders.
Results
During up to 38 years of follow-up, a 16% increased overall risk of mental disorders was observed in individuals exposed in utero to any maternal autoimmune disease (9.38/1000 person years) compared with their unexposed counterparts (7.91/1000 person years). The increased risk of overall mental disorders was observed for the five most common specific autoimmune diseases: type 1 diabetes (HR: 1.24, 95% CI 1.18-1.30), rheumatoid arthritis (1.25, 1.14-1.38), systemic lupus erythematosus (1.34, 1.13-1.60), multiple sclerosis (1.21, 1.08-1.36) and psoriasis vulgaris (1.24, 1.14-1.36). Regarding specific mental disorders, the highest risk was observed for organic disorders (1.54, 1.21-1.94), followed by schizophrenia (1.42, 1.22-1.66) and obsessive-compulsive disorder (1.42, 1.24-1.63), and a series of neurodevelopmental disorders (e.g., childhood autism [1.21, 1.08-1.36], mental retardation [1.19, 1.07-1.34] and ADHD [1.19, 1.12-1.26]).
Conclusions
Prenatal exposure to maternal autoimmune diseases was associated with increased risks of mental disorders in the offspring. These findings call for enhanced clinical awareness, monitoring and early intervention among children of mothers diagnosed with autoimmune diseases before or during pregnancy.

关键字 autoimmune disease, mental disorder, cohort study

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Association between childhood trauma and risk for obesity: a putative neurocognitive developmental pathway

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Background: Childhood trauma increases the risk for adult obesity through multiple complex pathways, and the neural substrates are yet to be determined.
Methods: Participants from three population-based neuroimaging cohorts, including the IMAGEN cohort, the UK Biobank (UKB), and the Human Connectome Project (HCP), were recruited. Voxel-based morphometry analysis of both childhood trauma and body mass index (BMI) was performed in the longitudinal IMAGEN cohort; validation of the findings was performed in the UKB. White-matter connectivity analysis was conducted to study the structural connectivity between the identified brain region and subdivisions of the hypothalamus in the HCP.
Results: In IMAGEN, a smaller frontopolar cortex (FPC) was associated with both childhood abuse (CA) (β = − .568, 95%CI − .942 to − .194; p = .003) and higher BMI (β = − .086, 95%CI − .128 to − .043; p < .001) in male participants, and these findings were validated in UKB. Across seven data collection sites, a stronger negative CA-FPC association was correlated with a higher positive CA-BMI association (β = − 1.033, 95%CI − 1.762 to − .305; p = .015). Using 7-T diffusion tensor imaging data (n = 156), we found that FPC was the third most connected cortical area with the hypothalamus, especially the lateral hypothalamus. A smaller FPC at age 14 contributed to higher BMI at age 19 in those male participants with a history of CA, and the CA-FPC interaction enabled a model at age 14 to account for some future weight gain during a 5-year follow-up (variance explained 5.8%).
Conclusions: The findings highlight that a malfunctioning, top-down cognitive or behavioral control system, independent of genetic predisposition, putatively contributes to excessive weight gain in a particularly vulnerable population, and may inform treatment approaches.

关键字 Childhood trauma, Adult obesity, Neurocognitive control pathway, Structural brain imaging

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Robust Prediction of Social Recognition Performance from Brain Structural Connectome in Children with Neurodevelopmental Disorders

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Objective: To identify a brain-based predictor of social recognition (SR) performance using a recently developed machine learning approach, connectome-based predictive modeling (CPM). Considering that CPM belongs to linear regressions, the present study enrolled participants with neurodevelopmental disorders and healthy controls to ensure adequate variability in the data in order for CPM to pick up brain-behavior associations.

Methods: Diffusion tensor magnetic resonance imaging scans and neurocognitive scale data were collected from 95 children and adolescents (age range, 6-16 years), 31 with autism spectrum disorder (ASD), 34 with attention-deficit/hyperactivity disorder (ADHD), and 30 age- and sex-matched typically developing (TD) individuals. Diffusion tensor imaging (DTI) and probabilistic tractography were used to construct whole-brain structural connectivity (SC) matrices, CPM based on the SC data was then used to predict the SR scores, which were measured by Social Responsiveness Scale (SRS). In the CPM pipeline, Pearson correlation between each brain connection in the SC matrices and SR scores were calculated across the participants, and the values were separated into a positive network and a negative network. CPM with leave-one-out cross-validation (LOOCV) was conducted to train linear models to respectively relate positive and negative network strengths to SR scores in the training set, each left-out testing subject’s strengths of positive and negative network was normalized using the parameters acquired during the training set, and then the trained models were used to predict the testing participant’s SR score.

Results: The correlation between the observed SR scores and predicted SR scores represents the predictive efficacy of each network. Results indicated that the positive and negative SR networks all significantly predicted individual differences in SR (positive SR network: $r = 0.14$, $p = 0.05$; negative SR network: $r = 0.16$, $p = 0.05$). Additionally, we found that the key connections between the prefrontal lobe (i.e., right superior frontal gyrus (orbital part), bilateral inferior frontal gyrus (orbital part) and bilateral olfactory cortex) and the temporal lobe (i.e., left middle temporal gyrus, right superior temporal gyrus and bilateral hippocampus) tended to contain most of the positive edges.

Conclusions: Our findings potentially help to understand the relationship between areas with a correlated cortical structure and social recognition, and further help to reveal the brain underpinnings related to its disorders.

关键字 Social Recognition, Structural Connectome, Neurodevelopmental Disorders, Connectome-Based Predictive Modeling

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Decreased inter-brain neural synchrony in autism during parent-child interaction-an EEG hyperscanning study

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Background：
Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairments in reciprocal social interaction, communication and repetitive stereotypic behavior. Deficits in social interaction are considered as most central to the disorder. Previous studies exploring the neural mechanisms of social deficits mainly focus on the brain activity of a single person during computerized social tasks rather than exploring interpersonal neural synchronization during social interaction. Thus, these studies might fail to reveal some core features of ASD. Considering that ASD is a neurodevelopmental disorder, many studies have sought to elucidate the neural basis by linking specific social deficits to dysfunction at specific brain regions. Neuroimaging work has shown that the components of social processing are linked to a social brain network including the temporoparietal junction (TPJ), the medial prefrontal cortex (mPFC) and the posterior cingulate cortex. Currently, it remains unclear how autism affects the development of the social brain networks implicated in the processing of social information at early developmental stages.
Methods：
A total of 28 children with ASD and 34 matched typically-developing (TD) children, aged between three and seven years, participated in the study with their parents. Diagnosis of ASD was rigorously verified and confirmed with Childhood Autism Rating scale(CARS) and Autism Diagnosis Observation Schedule-Generic (ADOS). Here, electroencephalography (EEG) signals were simultaneously measured from parent-child pairs during a live joint play task. In this task, each child played construction toys with the parent and the play session was videoed using two camcorders positioned next to the child and parent, respectively.The behavior patterns of parents and children in each seconds were manually coded by reviewing the video recordings using video editing software. The inter-brain neural synchronization in parent－child was calculated using Phase Locking Value (PLV) in theta EEG band for 9 regions-of-interest. Regions were selected so that left, midline, and right portions of frontal, central, and posterior scalp were represented during analysis. Next, we sought to establish the relationship between PLV and behavior patterns of ASD.
Results：
The present study found the Children's /Parents' Initiation (CPI,%) of ASD pairs was significantly lower than that of TD group. And the children with ASD had lower Initiation Frequency of Children(IFC, /min) than TD children.We also found that children with ASD showed decreased inter-brain neural synchronization in posterior regions when engaging in cooperative interactions with their parents than TD group. Further analyses of brain-behavioral relationships within the ASD group suggested that the neural synchronization was modulated by the children’s behavior performance (CPI and IFC). During live interactions, the decrease in synchronicity was associated with the lack of active initiation in children.That is, children with

severer social deficits showed lower level of action and neural synchronization with their parents during joint play task.
Conclusion：
In the present study, inter-brain communication between children with ASD and their parents was investigated in a socio-interactive context using EEG hyperscanning technique. Combined with the behavioral performance of children, the study confirmed the relationship between decreased parent-child inter-brain synchronization and the less initiating behavior of children with ASD in live interpersonal interactions. These results showed children with ASD had deficit of social networks in posterior brain. In conclusion, the EEG hyperscanning paradigm used in our study constitutes a promising opportunity to model the underlying neural mechanisms of social interaction deficit in children with ASD.

关键字 ASD, inter-brain synchronization, EEG，hyperscanning

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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The preterm infants motor development of associated factors based on the Alberta Infant Motor Scale

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【Abstract】 Objective: To evaluate the exercise of premature babies through The Alberta Infant Motor Scale (AIMS) to explore the associated factors of the motor development of premature infants and the relationship between exercise level and development quotient. Methods: selected 206 premature babies born from November 1, 2018 to March 31, 2019 and followed continuously by the Children's Health department of the hospital (37 weeks< of gestational age) and analyzed their corrective 6 months of age The relationship between AIMS exercise scale results and their gender、mode of birth、gestation、fetus number、the birth order、birth weight, father's education, mother's education, 6 months old weight, height, head circumference, 1 year old of DQ. Results: The univariate analysis showed that the level of motor development and birth weight of premature infants at 6 months of age (F-1.600, P-0.045), gestation (F-8.309, P-0.004), father's education (F-1.591, P-0.048), 6 months old weight (r-0.163, P-0.020), height (r-0.174, P-0.012), head circumference (r-0.170, P-0.015), 1-year-old DQ (r-- 0.364, P<0.001) have a certain relationship, and the multiple linear regression analysis shows that gestation (P-0.042) was the main associated factors of the development of premature babies' movement, but there is no significant influence on the maternal perinatal status and mother's education factors. Conclusion: The suspect motor development of premature babies is mainly related to the gestation, it may have some relationship with parent's education and 6 months old physical growth, but not with the maternal perinatal status, and AIMS can combine the child development Screening Test (DST) to monitor the premature in order to evaluate and intervene in time to promote the normal development of their movement.

关键字 premature; motor development; Associated Factors

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Vitamin A supplementation ameliorates autism-like behaviors in a valproic acid-induced rat model of autism

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Introduction: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social deficits and repetitive stereotyped behaviors. Prenatal exposure to an anticonvulsant drug valproic acid (VPA) is reported to induce ASD in human and ASD-like phenotypes in rodents. Unfortunately, the etiology and pathogenesis of ASD remains unclear.
Methods: Pregnant rats received an intraperitoneal injection of 600 mg/kg VPA on E12.5 to construct the ASD rat model in offspring. Different expression of long non-coding RNA (lncRNA) and mRNA profiles in the hippocampus were determined by RNA sequencing to investigate the potential mechanism of VPA-induced ASD. Gene Ontology (GO) and pathway enrichment analysis were performed to predict the function of the dysregulated lncRNAs. Co-expression network analysis and real-time polymerase chain reaction (RT-PCR) were conducted to validate the potential regulatory network of lncRNA-mRNA axis.
Results: VPA increased the total distance, time spent in the central zone and self-grooming (open field test). Meanwhile, VPA induced social impairment (three-chamber sociability test) and repetitive behaviors (marble burying test). A total of 238 lncRNAs and 354 mRNAs were differentially expressed in the VPA group. In addition, the dysregulated lncRNAs were involved in neural function and developmental processes of ASD. 5 lncRNAs and 7 mRNAs were differently expressed and included in the lncRNA-mRNA co-expression network. RT-PCR confirmed the upregulation of 4 lncRNAs and 6 mRNAs, and the potential regulatory network of the lncRNA NONRATT021475.2 and Desert hedgehog (*Dhh*) gene. Moreover, VPA decreased the serum vitamin A (VA) levels of offspring rats on postnatal day (PND) 21 and 49. While VA supplementation significantly restored the VPA-induced autism-related behaviors, and the upregulation of NONRATT021475.2 and *Dhh* in the hippocampus of ASD rats.
Conclusion: This study not only contributes to understand the importance of lncRNAs and mRNAs in the progression of ASD, but also identifies VA as a potential therapy.
Acknowledgement: Project supported by the National Natural Science Foundation of China [81671359, 8210120952], Natural Science Foundation of Jiangsu Province [BK20211017].

关键字 Autism spectrum disorder; Co-expression network; Long non-coding RNA; Valproic acid; Vitamin A;

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The current situation of preterm infants' motor development and its influencing factors based on the Alberta Infant Motor Scale

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Objective: To explore the current situation of preterm infants' motor development and analyze the possible influencing factors during the first months, so as to provide basis for constructing early motor intervention model for premature infants after discharge. **Methods:** Preterm infants born between November 2018 and March 2019,who were documented in the Child Healthcare Department of West China Second University Hospital,were enrolled in this study, the infants' AIMS-score at 3 months corrected age (CA) was used as the outcome indicator of motor development. **Results:** Among 361 preterm infants, 311 (86.1%) showed normal motor performance with AIMS score >P25;40 (11.1%) showed suspect motor performance with AIMS score P11 to P25 ;10 (2.8%) showed atypical motor development or motor delay with AIMS score≤P10. Logistic regression analysis showed that weight at 3 months CA (OR=2.883)was a protective factor, male (OR=0.415) was a risk factor, and the third parity OR above (OR=0.308)was a protective factor for motor development of preterm infants. **Conclusion:** The early motor development of preterm infants after discharge were generally good, however it is necessary to pay more attention to the preterm infants who are boys or with fewer parity, especially that with slower body weight catch-up.

关键字 Preterm infant; Child Development; Alberta Infant Motor Scale; Influencing Factors
早产儿；儿童发育；AIMS 量表；影响因素

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Atomoxetine: An updated review of its mechanism of action, clinical efficacy, safety and dosage regimen to children with ADHD

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Atomoxetine, a selective norepinephrine (NE) reuptake inhibitor, was approved for attention deficit/hyperactivity disorder (ADHD) treatment in children, adolescents and adults. Atomoxetine inhibits the presynaptic norepinephrine transporter (NET), preventing the reuptake of NE throughout the brain along with inhibiting the reuptake of dopamine in specific brain regions such as the prefrontal cortex (PFC). Therefore, it can increase the level of NE in the synaptic cleft and level of dopamine (AD) in the prefrontal cortex, enhance children's memory and attention, and significantly improve ADHD symptoms. It is mainly metabolized by the highly polymorphic drug metabolizing enzyme cytochrome P450 2D6 (CYP2D6). Atomoxetine is effective and generally well tolerated. Clinically meaningful improvements in the core symptoms of ADHD (inattention, impulsivity, and hyperactivity) as well as quality of life and emotional lability are often observed after atomoxetine treatment. Unlike stimulants, atomoxetine has a delayed onset to clinical effect and typically takes 2 - 4 weeks for full impact on symptoms to be observed. Similar to the findings in short-term studies, atomoxetine remained efficacious in the longer-term treatment of ADHD in children. However, few placebo-controlled, long-term studies of efficacy have been reported. Also, ADHD is often accompanied by multiple comorbidities. Co-morbid psychiatric disorders are common among patients with ADHD, including oppositional defiant disorder (ODD), anxiety and depression disorders, autism spectrum disorder (ASD), tics disorders (TD) and Tourette’s Syndrome (TS). More than two-thirds of children with ADHD have a co-morbid conditions. A series of studies have been published suggesting that atomoxetine is effective in the treatment of ADHD symptoms for children with various types of co-morbidity. In some cases, it is possible that atomoxetine may have a positive influence on the symptoms of comorbidities. In children with ADHD combined with transient tic disorder, atomoxetine treatment will not affect the secretion of dopamine and 5-hydroxytryptamine receptors in the body, effectively avoiding the aggravation of tic disorder and having high bioavailability. Atomoxetine may also be a first-line treatment for patients with comorbid tics. Currently, atomoxetine is only used in pediatric patients over 6 years old with ADHD. It can be administered either as a single daily dose or split into two evenly divided doses, has a negligible risk of abuse or misuse. In the process of treatment, clinicians should pay special attention to controlling the dose of atomoxetine. Generally, oral administration of atomoxetine to children can achieve better results. However, due to the relatively active or deficient CYP2D6 enzyme in some children, the absorption of atomoxetine will be affected to a certain extent. Adverse reactions were described from two aspects: common and rare adverse reactions. The most common adverse reactions of atomoxetine in children with ADHD include gastrointestinal (nausea, vomiting, decreased appetite, abdominal pain), sleep disturbances (somnolence), and other general disorders (Irritability, dizziness, fatigue). Based on previous research reports, liver injuries, suicidality, aggression/hostility, psychosis, seizures and prolonged QT interval are uncommon or rare. There is a small

but potential risk of QT interval prolongation. Rarely, atomoxetine may be associated with severe liver injury. The adverse reactions of atomoxetine were generally mild or moderate, and severe adverse events were quite rare. To have a more comprehensive understanding of atomoxetine, this review sets the focus on the mechanism of action, clinical efficacy and dosage in detail, and also touches on those studies regarding adverse reactions of atomoxetine.

关键字 Atomoxetine, ADHD, Children, Mechanism of action, Clinical efficacy, Dosage, Adverse reactions

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Gut microbial profile is associated with the severity of social impairment and IQ performance in children with autism spectrum disorders

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Background and Objective:
Autism spectrum disorders (ASDs) are highly heterogeneous with diverse symptom severity and comorbidities. Although the alterations of gut microbiota have been reported in ASD, it remains unclear whether specific microbial pattern contributes to certain aspects of symptoms or comorbidities in ASD. We aim to investigate the associations between gut microbiota and the severity of social impairment and cognitive functioning in children with ASD.

Methods:
A total of 261 age-matched children, including 138 ASD, 63 DD/ID (developmental delay or intellectual disability) and 60 TD (typical developing) children, were enrolled from Shanghai Xinhua Registry. The ASD children were further classified into two subgroups, 76 ASD with developmental disorder (ASD+DD) and 62 ASD-only. Gut microbiome was profiled and evaluated by 16S ribosomal RNA sequencing.

Results:
We characterized the gut microbiota demonstrating the presence of an altered microbial community structure in ASD children. The alpha diversity indices of ASD+DD and ASD-only subgroups were significantly lower than DD/ID or TD group. At the genus level, we observed a decrease in the relative abundance of Prevotella, while Bacteroides and Faecalibacterium were significantly increased in ASD children comparing DD/ID and TD subjects. There was a clear correlation between alpha diversity and the CARS total score in all subjects, and this correlation is independent of IQ. Similar correlations with CARS total score were also observed for Bacteroides, Faecalibacterium, and Oscillospira. However, there was no single genus significantly associated with IQ in all subjects.

Conclusions:
Specific alterations of bacterial taxonomic composition as well as the associations to the severity of social impairment and IQ performance were observed in children with ASD or ASD subgroups, when comparing to DD/ID or TD groups. These results illustrated that gut microbiota may serve as one of the promising biomarkers for ASD symptoms, however, warrant further investigations.

关键字 Autism, gut microbiota, 16sRNA, developmental delay/intellectual disability, intelligence

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Analysis of the current situation and influencing factors of exclusive breastfeeding rate of preterm infants at the age of 6 months

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Objective: To understand the current situation of exclusive breastfeeding of preterm infants and analyze the relevant influencing factors, so as to put forward targeted intervention suggestions to increase the rate of exclusive breastfeeding of preterm infants.

Methods: 260 premature infants born from November 1, 2018 to March 31, 2019 and filed in the child health department of West China Second Hospital of Sichuan University were selected by random sampling. Through the child health care system, the basic data of preterm infants and their caregivers and breastfeeding from birth to corrected 6 months old, including gestational weeks, mode of production, parity, parity, number of births, birth weight, mother's education, father's education, etc. Spss22.0 was used for data entry and analysis, the constituent ratio or rate was used for statistical description, the X^2-test was used for single factor analysis, and the non conditional binary logistic regression model was fitted for multivariate analysis.

Results: The results of this study showed that among 260 premature infants, 72 (27.69%) were exclusively breastfed to the corrected age of 6 months; The effects of birth weight and number of births on the corrected 6-month-old exclusive breastfeeding rate of preterm infants were statistically significant (P< 0.05). The exclusive breastfeeding rate of singleton infants was 3.614 times higher than that of multiple infants, and the heavier the birth weight (OR=1.557,P=0.003) and the fewer the number of births (OR= 3.614,P=0.00), the higher the exclusive breastfeeding rate.

Conclusion: There is still a big gap between the results of this study and the 50% exclusive breastfeeding rate required by the outline of China's child development (2011 ~ 2020). The exclusive breastfeeding rate of preterm infants corrected to 6 months old needs to be improved, especially the preterm infants with lower birth weight and more births; In the future, comprehensive management measures can be taken to improve the pure breastfeeding rate of 6-month-old preterm infants from multiple aspects by accelerating the construction of breast milk bank in neonatal Pediatrics, paying attention to the training of oral feeding of preterm infants, and strengthening the guidance of mother infant separation and lactation related knowledge; There are still some deficiencies in this study, such as the sample size and relatively few influencing factors. Future research can further explore the influencing factors of pure breastfeeding rate of preterm infants from multiple perspectives, such as expanding the sample size, the physical and mental status of preterm infants' mothers and the situation of preterm infants during hospitalization.

关键字 preterm infants; exclusive breastfeeding; influencing factors

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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A study on the features of consonants error in preschool and school-age dysarthria children

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Objective To analyze the features of consonants error in preschool and school-age dysarthria children, so as to provide evidence for clinical evaluation and treatment (guidance).
Methods Children diagnosed with dysarthria in the department of Child Health Care, West China Second University Hospital, Sichuan university, from Jan. 2014 to Jun. 2020 were enrolled. A retrospective investigation was conducted with phoneme evaluation to detect the types and characteristics of children consonants errors, and the characteristics of gender, age distribution were also explored.
Results Totally, 1141 dysarthria children were enrolled in this study, involving 877 boys and 264 girls, the male to female rate was 3.32:1, the gender difference was statistically significant (X2=323，P ＜ 0.01)；the age at diagnosis was 3~13(4.56±1.47) years old, and no significant difference was find between boys and girls (boys 4.57±1.49 years, girls 4.52±1.44 years, F=0.039，P ＞ 0.05). The main onset age of subjects in this study was 3~5years, accounting for 63.7%; the number of diagnosed cases gradually reduced with increasing age; the incidence of consonant errors in different pronunciation patterns was 81.5% for plosive, 39.6% for nasal, 79.8% for fricative, 81.9% for affricate, 59.0% for lateral. Cases with more than three kind of consonant errors accounting for 75.4%. Along with the age growth, the consonant error rate was gradually reduced (P ＜ 0.05). The incidence of nasal errors in boys was higher than that in girls (X2=5.002、5.557，P ＜ 0.05), but the gender difference was no statistically significant in plosive, fricative, affricate, lateral errors (P ＞ 0.05). **Conclusion** The preschool and school-age children with dysarthria had the highest incidence of affricate errors and the lowest incidence of nasal sounds, considering that it may be related to the development law of children's oral motor function and the regional linguistic environment. Dysarthria will be improved with the age growing, but some can not be completely self-healing. Therefore, the intervene measure should be implemented as early as possible to prevent children’s social and psychological barriers caused by dysarthria.

关键字 Dysarthria; Consonant Error; Children; Phonetic Feature.

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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A nomogram based on eosinophils for predicting the probability of food allergy in infants with feeding problems and malnutrition

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Background: Peripheral blood eosinophil (EOS) have been developed to raise the awareness of some allergic diseases. However, the relationship between EOS and food allergy in infants have never been reported. The aim of this study was to construct a nomogram based on eosinophils to predict the probability of food allergy in infants with feeding problems and malnutrition.
Methods: A multi-center study was conducted between August 2018 to December 2020. A total of 289 infants with feeding problems and malnutrition were included. A predesigned questionnaire and Cow’s milk-related symptom scores (CoMiSS) were used to record the information and eosinophils in peripheral blood were measured in each patient. The infants were confirmed of having food allergy via oral food challenge (OFC)/skin prick test (SPT). Risk factors for food allergy were identified by multivariate logistic regression analysis and used to create a nomogram. The performance of the nomogram was evaluated by using a bootstrapped-concordance index and calibration plots.
Results: 249 (86.2%) infants were diagnosed with food allergy in these infants. After adjusting for the confounding factors, compared with EOS percentage (EOS%) < 3%, the odds ratios (ORs) for food allergy diagnosis were 3.108 (1.182, 8.167), 5.774 (1.928, 17.295) and 11.969 (2.573, 55.669) when EOS% was 3-5%, 5-8%, and ≥8%, respectively. EOS%, feeding patterns, allergy family history and CoMiSS score were identified as a significantly associated factors that could be combined for accurate prediction of food allergy. We created a nomogram for food allergy by using these risk factors. The area under the curve (AUC) was 0.882 (95% confidence interval 0.819-0.946). The nomogram had a bootstrapped-concordance index of 0.882 and was well calibrated.
Conclusion: EOS% was significantly and positively associated with food allergy. Our nomogram was a useful tool for precise prediction of food allergy in infants with feeding problems and malnutrition.

关键字 the probability of food allergy, peripheral eosinophils, infants with feeding problem and malnutrition, nomogram

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Correlation between temperament characteristics and motor development level in premature infants

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Abstract: Objective: To study the relationship between temperament type and motor development level of premature infants by means of temperament type assessment and AIMS motor assessment. Methods: A total of 103 preterm infants (gestational age < 37 weeks) who were born from November 1, 2018 to March 31, 2019 were randomly selected and followed up in the Department of Child Care of our hospital. The results of preterm temperament assessment and the relationship between AIMS motor Scale results at 3 months and 6 months of age were analyzed. Results: There was no significant correlation between temperament type of preterm infants and motor development level at 3 months of age (P > 0.05). It was correlated with the motor development level at 6 months of age (P < 0.05). The AIMS motor assessment score of troubled preterm infants was significantly lower than that of plain preterm infants. Conclusion: as the growth of the aged, premature babies their motor development level have certain relations with different temperament types, premature type temperament type is relatively common trouble occurred more bradykinesia, understand the characteristics of premature infant temperament type is helpful to premature infant motor development ability and its development trend in the development of over months early prediction and promote the normal development of premature movement.

关键字 Key words: premature infant, temperament type, motor development

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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An Acceptance Analysis of the International Guide for Monitoring Child Development (GMCD) for Child Health Care Services in China

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Background: Developmental difficulties are broadly defined as a series of chronic health conditions caused by an impairment in language, learning, physical, or behavioral areas. These conditions occur whilst growing and developing, and may have a significant impact on children's health, functioning, and school achievement. A great deal of scientific research proved that early monitoring and screening are efficient ways to identify children with developmental difficulties and are also regarded as one of the most significant parts of child health services. Early childhood monitoring and screening enables pediatric health care providers to detect children's developmental risk factors or abnormal behaviors as well as reducing the risk of the onset of such diseases, the occurrence of disability, and promote early childhood development.

The International Guide for Monitoring Child Development (GMCD) is a family-centered method for monitoring child development based on biological and ecological theories and children's neuropsychological development milestones. As a package of child development monitoring, support, and intervention, GMCD was introduced to China in 2017 and has completed the localization of the toolkit, training authorization, and trainer's certification. A total of 158 pediatric health care providers have participated in the training and obtained certificates till September 2020.

The purpose of this study is to investigate the acceptance of GMCD in Chinese pediatric health care providers, to analyze the feasibility and applicability of the GMCD implementation in child health care services, and to provide an evidence-based basis for the promotion of GMCD in China.

Method: An online questionnaire was conducted among the GMCD trainees in China from July to December 2020. The survey mainly covered four aspects, including the satisfaction of GMCD toolkit content and structures, the advantages compared to other tools, the effects on improving the quality of pediatric clinic services, and effects on improving the competency of pediatric health care providers. Descriptive analysis methods were used to analyze those data.

Results: This data was obtained from 111 GMCD trainees, who worked throughout 75 child health care institutions in 16 provinces. Respondents were highly satisfied with the GMCD toolkit's content, and the satisfaction score of each domain were all above 80%. About 81.1% (90/111) respondents were satisfied with all six parts of the GMCD Toolkit, including the section of the introduction, questioning, coding, results explanation, intervention guidance, and a brochure named I learn with you. Most of the respondents agreed that the GMCD could improve the quality of pediatric outpatient services as well as the competency of pediatric health care providers, which accounted for 99.1% (110/111) and 98.2% (109/111), respectively. In addition, 92.8% (103/111) and 84.7% (94/111) of the respondents believed that the GMCD was able to enhance the initiative and trust of parental communication; furthermore, 91.9% (102/111) of respondents agreed that it can improve their communication skills with child caregivers.

One hundred and seventeen respondents also used other child development assessment tools in their daily work. Based on their feedback, the top three main advantages of

GMCD were no extra device required, ease of mastery, and high parental acceptance, which accounted for 81.3% (87/107), 74.8% (80/107), and 72.9% (78/107) respectively. **Conclusions:** GMCD has received a widely good reputation in child clinical health services in China. And it is suggested to be promoted nationwide to improve the quality of early childhood monitoring and screening services in children's psychological and behavioral development.

关键字 GMCD; pediatric health care providers; satisfaction

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Trends in Insufficient Sleep and Suicidal Behaviors among High School Adolescents by Age, Sex and Race/Ethnicity, 2007-2019

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Background
Suicide is worldwide public health priority, and has been increasing among US high school students. Insufficient sleep(<8h) is very common in this age group, and has been considered as an independent, proximal, and modifiable risk factor of suicide behaviors.Yet, it is unknown whether the trends in suicide behaviors differ between adolescents with and without insufficient sleep, and how social determinants of health (SDoH) across individual-level demographics may moderate the trends.
This study is aim to examine whether insufficient sleep is associated with trends in suicidal behaviors among US high school students from 2007 through 2019, and disparities by sex, age, and race/ethnicity subgroups.
Method
This cross-sectional study used data from the Youth Risk Behavior Survey (YRBS) from 2007 through 2019, a representative sample of US adolescents in grades 9 through 12. The analytic sample included 73 356 participants who answered the questions reporting past-year sleep duration(dichotomized into insufficient sleep[<8h] and sufficient sleep[≥8h]) and four suicidal behaviors(suicidal ideation, suicide plan, suicide attempts and injury by suicide attempt). Survey-weighted prevalence estimates, biennial percentage changes(BPCs) and average BPC in the survey-weighted prevalence of self-reported insufficient sleep and suicidal behaviors in each survey year. Trends of four suicidal behaviors were also stratified by sleep duration and sex, age, race/ethnicity, and intersectional terms(sleep duration*sex, sleep duration*age, sleep duration*race/ethnicity).
Results
Of 73 356 adolescents(mean[SD]age, 16.11[1.23] years), 37 574(weighted percentage, 50.03%[95%CI, 49.04%-51.01%]) were female. The weighted prevalence rate for insufficient sleep increased from 69.24%(95%CI, 67.14%-71.27%) in 2007 to 78.69% (95%CI, 76.96%-80.32%) in 2019—an average BPC of 1.06%(95%CI, 0.66%- 1.46%) for the entire period. There were increasing trends in suicidal ideation(BPC=2.88%, 95%CI, 1.65%-4.13%) and suicide plan(BPC=3.42%, 95%CI, 2.09%-4.77%) from 2007 to 2019. The trends in suicidal attempts and injury by suicide attempt increase from 2013 to 2019(BPC=2.25%, 95%CI, 0.83%-3.70%; BPC=2.24%, 95%CI, 1.25%-3.24%), after leveled trends from 2007 to 2013.
Joinpoint regression estimated that suicidal ideation and suicide plan in adolescents with insufficient sleep increased from 2007 to 2019(BPC=2.54%, 95%CI, 1.30%-3.79%; BPC=3.20%, 95%CI, 1.77%-4.64%), while the prevalence rates of suicidal ideation and suicidal plan in adolescents with sufficient sleep was stable. The trends of suicide attempts and injury by suicide attempt from 2007 through 2019 in both insufficient and sufficient sleep group remain stable.
Sex disparities was found in trends of suicide plan among adolescents with insufficient sleep, but not in adolescents with sufficient sleep. The female adolescents with insufficient sleep demonstrated consistent and significant increase in suicide plan from 2007 to 2019(BPC=4.03%, 95%CI, 2.47%-5.62%), but the prevalence

in male was stable between 2007 and 2019. Age disparities is only noted in the trend in suicide plan among adolescents with insufficient sleep, with older adolescents(BPC=3.56%, 95%CI, 1.89%-5.27%) had a higher increase in BPC than younger adolescents(BPC=2.31%, 95%CI, 0.70%-3.95%). Trends in suicide plan among the four racial subgroups with insufficient sleep demonstrated significant increases, with BPCs being highest for the White(BPC= 3.48%, 95%CI, 1.31%-5.69%), and lowest for the Hispanic(BPC= 1.18%, 95%CI, 0.15%-2.23%).
Conclusions
Adolescents with insufficient sleep showed consistently increased trends in suicidal behaviors. Older, female, Black and Latino adolescents who lack of sufficient sleep are at elevated risks of suicide. This study indicates sleep duration should be integrated to the suicide surveillance, and prevention and intervention strategies, especially for the most vulnerable populations.

关键字 Suicidal behavior, Insufficient Sleep，Adolescents

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Iron deficiency in early life is associated with altered brain activation patterns of cognitive control at age 10 years

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Background How perinatal iron deficiency (ID) affects the development of brain functions supporting high-order cognitive abilities is still unknown. We used task-based functional magnetic resonance imaging (fMRI) to evaluate brain activities during cognitive control in children aged 8-11 years with pre- and/or postnatal ID.
Method In a longitudinal birth cohort in China, the data of task-based fMRI and computer-based behavioral tasks were collected in 68 children aged 8-11 years with early (pre-and/or postnatal) ID or non-ID. The data from 44 children (mean age 9.95±0.98 years) were finally analyzed, with 22 early ID children and 22 non-ID children. The behavioral tasks performed in the fMRI scanner include proactive and reactive conditions. Proactive condition allowed participants to select the rule of a trial before the onset of targets, while the rule could not be selected until the onset of targets in reactive condition. Cue- and probe-elicited brain activities were recorded by fMRI when children performing the tasks. Linear mixed modeling was used to analyze the accuracy and reaction times of behavioral tests. For neuroimaging data, the 3dlme in AFNI was used to analyze the main effects of group (early ID vs. non-ID), condition (proactive vs. reactive), and their interactions in predicting cue- and probe-elicited brain activity.
Results Both accuracy (87.9±8.6% vs. 90.3±7.0%) and reaction times (1504.97±319.95ms vs. 1389.28±329.46ms) of behavioral tasks had no significant differences in early ID group vs. non-ID group ($p>0.05$). However, there were group differences in cue-elicited brain activity between proactive vs. reactive conditions at 6 brain clusters (Table 1; Figure 1), and such group differences were found at 14 brain clusters (Table 2; Figure 2) in probe-elicited brain activity between two conditions. These clusters involved brain regions from various circuits, including prefrontal cortex, parietal lobe, inner side of occipital lobe, temporal lobe, insula, and limbic system. Further analyses indicated that early ID and non-ID children showed different activation patterns at these brain regions in processing the tasks in proactive vs. reactive conditions.
Conclusion Prenatal and/or postnatal iron deficiency alters brain activation patterns of the circuits involving in cognitive control in school-aged children.

关键字 iron deficiency, children, brain development, cognitive control

Category: 4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Associations of in-hospital postpartum feeding experiences with exclusive breastfeeding practices among infants in rural Sichuan, China

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Abstract Content Exclusive breastfeeding rates are low in rural China, while the prevalence of formula use is high. Despite the knowledge that newborn feeding experiences in the hospital influence infant feeding practices later, rural hospitals reportedly do not follow recommended feeding guidelines to exclusively breastfeed newborns, even when accredited as baby-friendly. This study investigates the relationship between in-hospital feeding experience with current infant feeding practices in rural China.

Methods We used cross-sectional data collected in 2019 from 782 caregivers of infants 0 to 6 months in four nationally designated poverty counties in Nanchong Prefecture, Sichuan, on demographic characteristics, current infant feeding practices, and in-hospital postpartum feeding experiences. Six categories of current feeding practices (exclusive breastfeeding, predominant breastfeeding, mixed feeding, mixed feeding with solids, no breastfeeding, no breastfeeding with solids) were created based on a 24-hour dietary recall. Then, using adjusted multivariate logistic regression, we predicted current feeding group membership and estimated change in membership if hospitals followed baby-friendly feeding criteria, accounting for differences in participants' likelihood of in-hospital compliance.

Results Nearly 39% of infants were exclusively breastfeeding at the time of the survey, while 62% and 77.6% had been fed water and formula while in the hospital, respectively. We found that child age, caregiver type (mother or other), family wealth, delivery location, and hospital feeding experiences predicted current feeding practice category. Simulation results suggest that if hospitals follow baby-friendly feeding guidelines, exclusive breastfeeding group membership will increase to 53.1% (95% CI: 45.9, 60.3).

Conclusion Given the importance of an infant's first feeding experiences on later exclusive breastfeeding practice, it is critical for rural Chinese hospitals to improve their practices by eliminating water-based feeds and limiting formula feeds to only medically indicated situations. The next step of this study is to examine the model fit using newly obtained data from 768 families in 2021. The new data shows that around 34% of infants were breastfed exclusively at the survey, while 50% of infants were fed water and 87% were fed formula postpartum in the hospital. A goodness of fit test will be conducted to see if the newly observed values match those predicted by our existing model.

Key words Postpartum hospital practices, infant feeding, breastfeeding, rural China
Reference N/A

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Risk of ASD and ADHD in Migrant Children: A Systematic Review and Meta-analysis

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Purpose
Migration has been implicated as a risk factor for autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD), but evidence is limited and inconsistent. We conducted a systematic review with meta-analysis to investigate the relationship between migration status and risk of ASD and ADHD.
Method
We searched PubMed, EMBASE, Web of Science Core Collection, and PsycINFO, for epidemiological studies that measured the association between migration status (migrant group versus non-migrant group) and risk of ASD or ADHD in children from database inception to February, 2021. Migrant children were defined as 1) the children who moving away from the place they live, or 2) the children had one or more parent born aboard. The methodological quality of included studies was assessed using the Newcastle-Ottawa Quality Assessment Scale (NOS). Priori Der-Simonian and Laird random-effects model was used to estimate pooled OR (odds ratio) with 95% CI for ASD or ADHD. Between-study heterogeneity was tested using I2 statistic, and an I2 ≥ 50% was considered to represent high heterogeneity. Subsequently, subgroup analyses were carried out stratified by ASD comorbid intellectual disability, migration generation, parental country of birth, and NOS score. Publication bias was detected using Egger’s and Begg’s tests. All analyses were conducted using Stata software version 11.0, and P value < 0.05 inferred the statistical significance.
Results
After excluding duplicates, abstracts sifting, full texts reviewing, and manual searching, 17 eligible studies (eight cohort studies, seven case-control studies, and two cross-sectional studies) were finally included in this systematic review and meta-analysis. The NOS score of 15 eligible studies reached 7.
13 studies reported the association between migration status and risk of ASD. Compared to non-migrant children, the pooled OR for ASD among migrant children was 1.32 (95% CIs: 1.07－1.63, P = 0.010) with a high heterogeneity (I2 = 87.6%). Subgroup analyses indicated that migrant children were more likely to develop ASD comorbid intellectual disability (pooled OR: 1.21, P for interaction = 0.006). Stratified by parental country of birth, migrant children with foreign-born mother had a significant increased risk of ASD (pooled OR: 1.49; 95% CIs: 1.19－1.87). No significant interaction was observed stratified by NOS score (P for interaction = 0.739).
Six studies reported the association between migration status and risk of ADHD. The pooled OR for overall migration was 0.84 (95% CIs: 0.53－1.32, P = 0.452) with a high heterogeneity (I2 = 70.2%). Subgroup analyses indicated that migrant children with foreign-born mother were at lower risk of ADHD, on the contrary, migrant children with foreign-born father might at higher risk of ADHD (pooled OR were 0.92 and 1.58, P for interaction = 0.008). No significant interaction was observed stratified by generation of migration and NOS score (P for interaction were 0.726 and 0.271). Significant publication bias was detected in pooled estimates for ASD. After recalculated OR using the trim-and-fill method, increased risk for ASD in foreign-

born mother subgroup was still observed (imputed OR: 1.11; 95% CIs: 1.03 - 1.21; P = 0.007). No significant publication bias was detected in pooled estimates for ADHD.
Conclusion
Comparing to non-migration status, maternal migration was associated with increased risk for ASD, and migrant children were more susceptible to ASD comorbid intellectual disability. Although no significant association was observed between overall migration status and ADHD risk, maternal and paternal migration might be differently associated with risk of ADHD. Given to the children in such position might suffer social injustice and unbalanced medical resources, health care practitioners should consider screening and providing extra resources for migrant children.

关键字 ASD; ADHD; Migration; Systematic Review and Meta-analysis

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Serum hepcidin is a predominant predictor of iron deficiency anemia in preterm infants

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Background: Iron deficiency and iron deficiency anemia are widespread in low-income countries, particularly among preterm infants. No specific indicators are available for the early diagnosis of iron deficiency in preterm infants. Hepcidin is a key regulator of iron metabolism, which offers the possibility of new solutions to diagnose iron deficiency in premature infants. However, the sensitivity and specificity of hepcidin in the early diagnosis and treatment of iron deficiency anemia in premature infants has not been fully understood.
Objective: To study the value of serum hepcidin in the early diagnosis of iron deficiency.
Subjects/Methods: In a prospective observational study, serum hepcidin was ananlysed in 77 infants with gestational age from 28+1 to 36+6 weeks within the first 6 months of life. Infants were stratified according to iron status indicators and divided into 2 groups: iron deficiency (ID)and no iron deficiency.
Results: Mean serum hepcidin levels were significantly lower in premature infants with ID than those without ID. A single-variate linear regression model was used to explore the correlation between iron hepcidin and other indicators of iron metabolism. Serum hepcidin was positively correlated with birth weight, length of birth, SI, SF and daily iron supplementation in premature infants($p < 0.001$), and negatively correlated with total iron binding capacity($p < 0.001$). logarithmic ferritin showed the strongest positive correlation with logarithmic hepcidin ($p < 0.0001$).
Conclusions: ID preterm infants have lower serum hepcidin levels than those without ID preterm infants. Hepcidin can be used as an efficient indicator of iron storage in the body and a promising indicator for the early diagnosis of iron deficiency in premature infants.

关键字 hepcidin; iron deficiency; preterm infants

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Snijders Blok-Campeau syndrome caused by CHD3 gene mutation: a case report

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Objective: We report a case of Snijders Brok-Campeau Syndrome caused by CHD3 gene mutation, which is the first case in China,and summarize the clinical characteristics and review the literature.
Results: A boy of five months old was found that his motor development lagged behind for 1 month. Physical examination: the head circumference was 46.5cm, the head was slightly instability and can be raised in prone position, but he could not turn over. Cranial MRI: delayed myelination, widening of bilateral anterior ventricles, sharp posterior body, widening of bilateral frontotemporal space, extremely obvious temporal and thin pressing part of corpus callosum. Gesell development scale: Adaptability: 53, moderate growth retardation; Large movement: 51, moderate growth retardation; Fine motor: 54, moderate growth retardation; Language: 38, severe growth retardation; Person social: 62, mild growth retardation. His brother was diagnosed as ″Pseudo Fat Muscular Dystrophy (DMD)″, and his mother's amniocentesis during pregnancy: no deletion of exon 45-52 of DMD gene was found. No abnormality was found in the screening of biochemical items, blood gas, blood ammonia, thyroid function and hematuria metabolic screening . Cardiac ultrasound showed patent foramen ovale. MLPA detection of DMD gene: no copy number changes in relevant regions that can clearly explain the patient's phenotype detected. Whole exon gene detection: CHD3 gene mutation Exon21: C. 3535g > A (P. asp1179asn) was detected. This mutation is a new mutation, and his parents, brothers and sisters do not carry this mutation, so it is considered to be a pathogenic mutation. Related diseases: Snijders Brok-Campeau Syndrome is an autosomal dominant neurodevelopmental disorder characterized by overall growth retardation, intellectual development disorder and language acquisition disorder. Other features include big head deformity and characteristic facial features, such as prominent forehead, hypotonia and joint relaxation. No such cases have been reported in China.
Conclusion: Snijders Brok-Campeau Syndrome is an autosomal dominant disease, and the cases are rare. When children have large head deformity and overall growth retardation, they must be vigilant against this disease. All exon gene detection is helpful for diagnosis.

关键字 Snijders Brok-Campeau Syndrome, macrocephaly, CHD3 gene

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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A case report of ataxia caused by CTBP1 gene mutation

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Objective: To report a case with phenotype as hypotension, ataxia, growth retardation and enamel defect caused by CTBP1 gene mutation, which is the first case in China. To summarize the clinical characteristics and review the literature.
Methods: The clinical data and molecular genetic test results of a case of ataxia caused by CTBP1 gene mutation were analyzed retrospectively, and the relevant literature was analyzed.
Results: A girl was found walking unstable when she was 1.5 years old. She went to the local hospital and was given orthopedic shoes and intermittent rehabilitation treatment for half a year. The effect was not satisfying. When she was 2.5 years old, she went to our hospital, at that time she could take a few steps alone, slowly and unstable. Physical examination: head circumference was 48 cm, ataxia gait, muscle strength of both upper limbs IV+, muscle strength of both lower limbs IV, decreased muscle tension, weakened knee tendon reflex on both sides, and negative Babinski's sign on both sides. The birth history and family history were normal. Cranial MRI: bilateral cerebellar atrophy. Blood routine, biochemistry, lactic acid, homocysteine, blood ammonia, thyroid function, alpha fetoprotein, immunoglobulin and complement were normal. Hematuria metabolism screening was negative. Electromyography: no abnormality. Gesell development scale: DQ = 80, marginal level. All exon gene detection: it is analyzed that there is a heterozygous mutation in CTBP1 gene: C. 1024c > t (nucleotide 1024 in coding region changes from cytosine to thymine), resulting in amino acid change p.r342w (amino acid 342 changes from arginine to tryptophan), which is a spontaneous mutation. It is a pathogenic variation. Associated diseases: hypotension, ataxia, growth retardation and enamel defect syndrome. There is no report in China. A total of 12 patients were reported abroad with clinical manifestations as: overall growth retardation, ataxia, low muscle tone, slow weight growth, enamel defects.Phenotype appears in the first year after birth. Most of the cases are spontaneous mutations. The child was followed up to 4 years old and had enamel dysplasia, growth retardation, unstable walking and ataxia gait.

Conclusion: Hypotension, ataxia, growth retardation and enamel defect syndrome is an autosomal dominant disease which is rare. When children have ataxia, growth retardation and cerebellar atrophy, they should be vigilant against the disease. All exon gene detection is helpful for diagnosis.

关键字 ataxia, growth retardation, CTBP1 gene

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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High-Dose Iron Supplementation in Premature Infancy Modestly decreases Growth in an open real-world study

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Background: Iron deficiency and iron deficiency anemia are prevalent among preterm infants. However, there are few relevant studies about the therapeutic effect of iron supplementation in preterm infants.
Objective: To investigate the therapeutic effect of different doses of iron supplements in preterm infants.
Subjects/Methods: In an open real-world study, 143 preterm infants with gestational age from 28+1 to 36+6 weeks were stratified according to actual iron intake of preterm infants and divided into 3 groups: low-dose group [<1mg Fe/(kg • d) iron intake], medium-dose group [1-3mg Fe/(kg • d) iron intake], and high-dose group [≥3mg Fe/(kg • d) iron intake].
Results: There was no statistical difference between the iron status indicators and the various iron supplementation doses of preterm infants at the correction of gestational age of 3 months and 6 months. Statistically significant differences were observed in the length of premature infants given different doses of iron supplements. The mean length of the low, medium and high dose groups is 67.34, 67.68 and 65.84 cm ($p<0.015$). The weight gain of preterm infants in the high-dose iron group was significantly lower than that of the low-dose iron and medium-dose iron groups ($p = 0.048$). The average weight gain at the correction of gestational age of 3 months was 0.47, 0.38 and 0.21 kg in the low, medium and high dose groups. A Univariate regression analysis was used to explore the correlation between hepcidin and physical growth index of preterm infants. A negative correlation was found between weight gain, length gain and head circumference gain and logarithmic hepcidin levels in preterm infants ($p < 0.001$).
Conclusions: High-dose iron supplementation slightly reduces growth in premature infants, which may suggest that excessive iron supplementation may be detrimental to the physical development of premature infants.

关键字 Iron Supplementation; Premature Infancy; Iron deficiency; Iron deficiency anemia

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Development and norm development of an assessment scale for auditory processing in preschool children

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Objective To develop a auditory processing assessment scale for preschool children and establish the norm data of the scale, which can be used to screen preschool children at high risk of auditory processing disorder, so as to provide them with early referral evaluation, early auditory training and rehabilitation.

Method The construction process of the scale includes the following steps: ① construct the theoretical framework of the scale under the guidance of the theoretical model of auditory processing disorder; ② After literature review and qualitative interviews with parents, the scale item pool was preliminarily constructed; ③ After expert consultation and pre investigation of 20 small samples, the items of the scale were screened and revised to form the prediction version of the scale; ④ Through the pre investigation of 680 large samples, the scale items and exploratory factor analysis were carried out, and the items that did not meet the quality requirements were eliminated to form a formal scale; ⑤ Seven kindergartens were selected by stratified cluster random sampling, including 1419 preschool children from four kindergartens for reliability and validity analysis, and 1064 preschool children from three other kindergartens for confirmatory factor analysis; ⑥ Finally, the regional norm of the scale is established to provide a reference for the interpretation of the test results of the auditory processing evaluation scale for clinical preschool children.

Results The initially constructed item pool of the scale involves 54 items in 6 dimensions, and 37 items are retained after expert consultation. Through item analysis and exploratory factor analysis, a auditory processing assessment scale for preschool children with 5 dimensions (auditory decoding, auditory attention, communication, hyperactivity impulse and visual attention) and 30 items is formed; Cronbach's alpha of the scale was 0.941, and Cronbach's alpha for all dimensions ranged from 0.734 to 0.912, confirmatory factor analysis results show that: $x^2/df = 3.884$, RMSEA =0.052, GFI=0.909, CFI=0.923, TLI=0.913, IFI=0.924。 The scale norm data showed a skew distribution, and the scale percentage grade norm was established.

Conclusions The preschool auditory processing assessment scale has good reliability and is able to be used to screen preschool children at risk for auditory processing abnormalities, providing a reliable basis for referral assessment, differential diagnosis, and evaluation of training effectiveness by parents, otolaryngologists, developmental behavior physicians, and rehabilitation practitioners

关键字 Preschool children　Auditory processing　Scale　Norm

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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The effects of maternal 25-hydroxyvitamin D_3 deficiency on the risk of gestational diabetes mellitus

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Background: To investigate the association of maternal circulating 25-hydroxyvitamin D3 [25(OH)D3] levels with the risk of gestational diabetes mellitus (GDM), and explore the potential modification effect of maternal age in a prospective cohort study in China.
Method: 890 pregnant women underwent oral glucose tolerance test (OGTT) were randomly selected from the Shanghai Birth Cohort. Serum 25(OH)D3 levels were measured in both the first (T1) and second trimester (T2), using liquid chromatography-tandem mass spectrometry. Multiple logistic regression models were used for evaluating the association of vitamin D status and GDM. Subgroups analysis as well as interaction analysis were used for examining the modification effect of maternal age on the associations.
Results: Maternal vitamin D deficiency (25(OH)D3 < 20 ng/ml), especially in T2, lead to increased levels of fasting blood glucose (FBG) (P=0.005), but not 1h postload glucose (1h-PG) and 1h postload glucose (2h-PG) of OGTT. Furthermore, with the severity of vitamin D deficiency from T1 to T2, there was a progressive increase of FBG levels (P=0.012). Vitamin D deficiency in T2 was associated with a 1.66-fold increased risk of GDM (OR:1.66, 95% CI:1.01-2.73, P=0.044). Moreover, maternal age modified this effect on GDM (P for interaction=0.043), with a much higher risk among women aged ≥ 30 years (OR:3.76, 95% CI:1.69-8.35, P=0.001). However, no similar associations were observed among women with vitamin D deficiency in T1. Consistent vitamin D deficiency in T1 and T2 was not significantly associated with the risk of GDM, whereas it showed an increased risk of GDM to a marginal extent (OR:1.46, 95% CI: 0.76-2.81, P=0.260).
Conclusions: Vitamin D deficiency in T2, but not in T1, was associated with increased risk of GDM, and this risk was much higher among pregnant women aged ≥ 30 years.

关键字 Vitamin D deficiency; gestational diabetes mellitus; maternal age

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Association of maternal and fetal vitamin D with neurodevelopment at 2-year-old and the potential sensitive period: A prospective birth cohort study

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Abstract

Background: The link between vitamin D status and neurodevelopment has been suggested, but it remains unclear regarding the association between continuous change of maternal vitamin D status and offspring's neurodevelopment.

Objectives: This study aimed to explore the periodic and continuous effect of vitamin D status during pregnancy and at birth on offspring's neurodevelopment outcomes.

Methods: As part of the Shanghai Birth Cohort Study, 758 mother-infant pairs with complete data were selected. Concentrations of 25-hydroxyvitamin D [25(OH)D] were measured by the liquid chromatography tandem mass spectrometry (LC-MS/MS). Neurodevelopment was assessed at 2 years using Bayley Ⅲ scales. And information of confounding factors was collected by questionnaires. Univariate analysis and multivariable regression model were exploited to examine the associations between vitamin D status and offspring outcomes.

Results: Toddlers of the lowest 25(OH)D concentration group in late pregnancy exhibited a deficit of 8.68 (95% CI: -15.90, -1.45) in cognitive scores, and 5.94 (95% CI: -11.34, -0.54) in language scores, compared with the highest group ($p < 0.05$). And the similar association was also founded in cord blood when comparing the cognitive scores (β = -13.26, 95% CI: -19.07, -7.46), language scores (β = -6.71, 95% CI: -11.08, -2.33), and motor scores (β = -7.53, 95% CI: -12.12, -2.93) ($p< 0.05$). When considered of continuous change of maternal serum 25(OH)D, the mother whose serum 25(OH)D concentrations were below 30 ng/mL in all 3 trimesters, their offspring's cognitive subscale score was lower than others. Besides, the offspring of maternal 25(OH)D concentration once lower than 30 ng/mL in early or middle pregnancy had a higher risk of abnormal score in cognitive subscale of Bayley Ⅲ than those who did not (OR = 0.51, 95% CI: 0.26, 0.98 vs OR = 0.28, 95% CI: 0.13, 0.59) ($p<0.05$).

Conclusions: Our results provide evidences that the serum 25(OH)D concentrations in late pregnancy and at delivery were positive associated with Bayley Ⅲ scores of cognitive, language and motor subscales. And when considered of continuous effect, it's suggested that the serum 25(OH)D concentrations once below 30 ng/mL in early or middle pregnancy has negative effect on toddlers' cognitive scores. Further studies are warranted to confirm these findings and to investigate underlying mechanisms.

关键字 25-hydroxyvitamin D; Neurodevelopment; Pregnancy; Prenatal nutrition; Infant

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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Research Progress on Methods of Screening and Assessment of Adolescent Scoliosis

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Background: Scoliosis refers to a spinal deformity in which one or more segments of the spine bend laterally and are accompanied by vertebral rotation and kyphosis or lordosis changes in the sagittal plane. Adolescent idiopathic scoliosis has become the third "killer" of children and adolescents' health in Asia after obesity and myopia. Scoliosis in children and adolescents will not only cause external deformities such as hunchback, high and low shoulders, long and short legs, and asymmetric bone development but also cause organ development deformity and dysfunction. The purpose of this study is to elaborate on the current research progress on scoliosis screening and assessment methods and to provide a theoretical basis for the future application and selection of scoliosis.
Method: We used the literature data method to retrieve the currently commonly used or cutting-edge technical methods for adolescent scoliosis screening. These methods are divided into three categories, including the assessment based on two-dimensional images, three-dimensional images, and wearable sensors. The advantages and disadvantages of these three methods are horizontally compared, which will provide classification help for future youth scoliosis screening.
Result: The assessment based on two-dimensional images includes traditional medical images such as X-ray and MRI, moire grating images, and body surface images for feature extraction. This method determines the position of the spine through the image, to solve the abnormal posture of the spine, such as Cobb and trunk rotation angle. However, the disadvantages of this method are high-intensity radiation and unprotected privacy. The assessment based on 3D images includes depth camera, radar scanning, and ultrasonic reconstruction. By establishing a three-dimensional model of the spine, the evaluator can more intuitively observe the physiological structure of the adolescent spine. After continuous improvement of equipment and algorithms, this assessment method will show higher reliability and validity in the future. However, the equipment of this method is expensive and limited to places. Generally, it can only be completed in laboratories or hospitals. The assessment methods based on wearable sensing devices include optical fiber sensors, magnetic sensors, inertial sensors, and flexible strain sensors based on new materials. This method collects the spine activity of adolescents during exercise to monitor abnormal posture in real-time. In the meanwhile, the use of the wearable sensor is different from the acquisition of two-dimensional and three-dimensional images. It can monitor for a long time in any place and provide dynamic data support for evaluators.
Conclusion: The above assessment methods are of great significance for the screening of adolescent scoliosis. For the daily screening of adolescent spine posture, it is very important to control the development trend of scoliosis in the early stage. At the same time, for patients with scoliosis who have been diagnosed, only by accurately evaluating the current spinal morphology and course progress in the rehabilitation process, can we carry out the targeted intervention in the later stage, such as manual rehabilitation, brace correction, or surgical treatment, and finally achieve the purpose of improving the quality of life.

关键字 Adolescent scoliosis; Screening; Assessment

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Relationship Between SNAP-25 Gene Polymorphisms and Effects of Methylphenidate in Children With ADHD: an fNIRS Study

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Objective:Attention-deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder, methylphenidate (MPH) is the first-line drug for the treatment of ADHD,However, individual curative effects and adverse reactions are different.Studies have found that synaptosomal-associated protein 25 *(SNAP-25)* gene *Mn1I* polymorphisms is related to the efficacy and adverse reactions of MPH.However,the association between *SNAP-25Mn1I* polymorphisms and changes of brain hemodynamic responses after MPH treatment is still little understood.This study investigated the interaction of treatment-related hemodynamic changes with genotype status for the *SNAP-25* gene in children with attention-deficit hyperactivity disorder (ADHD) pre- and post- (MPH) treatment.
Methods:In total, 38 right-handed children diagnosed with ADHD were enrolled in this study. Clinical data, responses to SNAP-IV and adverse reaction questionnaires, and Intermediate Visual and Auditory Continuous Performance Test (IVT-CPT) scores were collected before and after 4 weeks of MPH treatment. Children were divided into two groups based on *SNAP-25* gene *Mn1I* polymorphisms and were behaviorally evaluated using the go/no-go test paradigm. Oxygenated hemoglobin (oxy-Hb) levels in the frontal cortex pre- and post-MPH treatment were monitored using functional near-infrared spectroscopy (fNIRS). Changes in cerebral oxy-Hb levels, effects of MPH treatment, and occurrence of adverse reactions were analyzed. Data were analyzed using IBM SPSS Statistics version 22. The Kolmogorov-Smirnov test was used to assess normality of data. Fisher’s exact test was used to compare categorical data. For normally distributed data, we performed two-tailed paired t-tests to compare post-MPH treatment vs. pre-MPH treatment values. Continuous variables and independent samples were compared using an independent samples t-test. For non-normally distributed data, the Wilcoxon signed rank test was used to assess independent samples, and the Mann-Whitney U-test was used to compare data between groups. Sex, age, therapy time, genotype, and [oxy-Hb] signals in each channel pre- and post-MPH treatment were analyzed using a generalized linear mixed model (GLMM). Statistical significance was set at $p < 0.05$.
Results:No significant differences were observed in baseline characteristics between T/T genotype and G allele groups. The T/T genotype group exhibited a significant decrease in SNAP-IV score after MPH treatment($p = 0.001$, 0.003, and 0.001, respectively) and significant increase in control auditory persistence quotient score in the IVT-CPT($p = 0.009$). SNAP-IV and IVT-CPT scores of the G allele group were not significantly different pre- and post-treatment. In the T/T genotype group, oxy-Hb levels in the dorsolateral prefrontal cortex were significantly higher post-treatment than pre-treatment. In the G allele group, no significant differences between pre- and post-treatment oxy-Hb levels were observed. In the go/no-go task, the accuracy of the T/T genotype group was significantly increased post-MPH treatment. No significant differences were observed in “go” response time (RT) and accuracy and no-go accuracy in the G allele group pre- and post-MPH treatment. No significant between-group differences were observed in the occurrence of adverse reactions.

Conclusions:In conclusion, in Asian children with ADHD, the *SNAP-25 MnlI* polymorphism may be associated with responses to MPH and may affect neurovascular coupling in the prefrontal cortex. Further, fNIRS combined with *SNAP-25 MnlI* polymorphism analysis in children with ADHD during go/no-go task performance may be a useful biomarker for evaluating the effects of MPH.

关键字 functional near-infrared spectroscopy, ADHD, methylphenidate, SNAP-25, Polymorphisms

分类：4. Child Health Care & Developmental Behavior 儿童保健与发育行为
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The Current Status and Influencing Factors of Screen Exposure in Children with Global Developmental Delay

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Background To investigate the current status of screen exposure in children with global developmental delay, and to explore the related factors affecting screen exposure time.
Method The data of 217 children with global developmental delay aged 2 to 4:11 years old who visited the Department of Developmental and Behavioral Pediatrics, Shanghai Children's Medical Center from November 2019 to June 2021 were collected. Their parents completed the screen exposure questionnaire. The screen exposure status was described. The risk factors of screen exposure of children with global developmental delay were analyzed by Logistic regression.
Results 80.2% of the children with global developmental delay had their onset age of screen use before 18 months-old and 51.6% of them use screen exceeding 1 hour per day. When contacted with the screen,37.3% primary caregivers choose to accompany more than half of the time. The Logistic regression analysis showed that high frequency of reading activities between primary caregiver and child (> 3 days per week) is the independent protective factors of screen exposure time exceeding 1 hour per day in children with global developmental delay. Not having mother as the primary caregiver and having screen exposure while eating are the independent risk factors of screen exposure time exceeding 1 hour per day in children with global developmental delay.
Conclusions The proportion that non-compliance with the screen guidelines of children with global developmental delay was high. Children's screen exposure time is affected by primary caregivers and their behaviors. Pediatricians should strengthen the propaganda of the correct way of screen use so as to prevent children from early and excessive exposure to screen.

关键字 global developmental delay； screen exposure； influencing factors

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Research progress in application of functional near-infrared spectroscopy in children's language development

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Background Functional near infrared spectroscopy(fNIRS) is an emerging neuroimaging technology. Compared to other neuroimaging technologies, fNIRS has many advantages: non-invasive, portable, robust to motion and acoustically silent. Therefore, it has important values in the research of children's language development.
Method To summarizes the research progress of fNIRS in children's language development, we searched for relevant articles in databases of PubMed, Embase and web of Science in recent five years.The following search terms were used: (a) (fNIRS) or (functional near-infrared spectroscopy) or(NIRS) or (near-infrared spectroscopy) (b) (language) or (speech) (c) (newborn*) or (infant*) or (child*) or (preschool*) or (school*)
Results At present, fNIRS has mainly been used in the research of neonatal word recognition, infant language perception, language functional lateralization, bilingual cognitive mechanism, language related neurodevelopmental disorders and so on.
Conclusions fNIRS has a bright future of applications in the field of children's language development.

关键字 Child language; Functional near-infrared spectroscopy; Word recognition; Language perception; Functional lateralization; Bilingual; Neurodevelopmental disorder

Endocrinology

内分泌遗传代谢

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Circulating miRNA profiles in patients with Down syndrome and identification of miR-29a-3p as a putative negative regulator of Aβ degradation

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This study is aimed to clarify the differential expression profile of miRNA in Down syndrome (DS) children and explore whether the target miRNAs are involved in the regulation of the production of amyloid β peptide (Aβ) in DS patients. MicroRNA expression profile in serum from DS was analyzed using miRNA microarray. Differentially expressed of interested miRNAs was further validated by qRT-PCR. Levels of plasma Aβ40 and Aβ42 in DS patients and healthy control (HC) group were determined by a double antibody sandwich enzyme-linked immunosorbent assay method, while insulin degradation enzyme (IDE) expression level was measured by RT-PCR. Correlation analysis of miR-29a-3p and IDE in DS and HC was done and the binding site was forecasted by the Targetscan. A total of 167 different miRNAs were discovered in DS and HC groups and 81 miRNAs were obviously up-regulated, while 86 miRNAs were down-regulated in DS group compared with HC group. The results of qRT-PCR for interested miRNAs were consistent with microarray data. Levels of Aβ40, Aβ42 and IDE expression were significantly higher in DS group than those in HC group. In addition, expression level of miR-29a-3p was negatively correlated with IDE. Targetscan predicted that 3' UTR of IDE has binding sites for miR-29a-3p. In conclusion, our results demonstrated that deregulation of miR-29a-3p and its target IDE may be involved in the Aβ production process for DS. Our findings provide a clue to study the underlying molecular mechanisms in DS patients,especially the development of neurodegenerative disease in DS patients.

关键字 Circulating miRNA profiles; Down syndrome; amyloid β peptide degradation; MiR-29a-3p; Insulin degradation enzyme

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Genotype and phenotype analysis of a case of Congenital anomalies of kidney and urinary tract syndrome with or without hearing loss, abnormal ears, or developmental delay caused by PBX1 mutation and literature review

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Abstract Objective To Investigate the genotype and phenotypic characteristics of the congenital anomalies of kidney and urinary tract syndrome with or without hearing loss, abnormal ears, or developmental delay (CAKUTHED) caused by PBX1 mutation, and to improve the understanding of the disease. Methods The clinical manifestation and clinical exon sequencing performed on Trio testing model were retrospectively analyzed. The relationship between genotype and phenotype and the treatment and follow-up of the child for 3 months were summarized. According to HGMD, PubMed, Wanfang and CNKI, relevant literature was reviewed to elaborate the possible pathogenesis of the pathogenic gene. Results The child was 4 years and 2 months old. He was refered to our hospital for “short stature″, accompanied with special facial appearance, low renal value, enhanced renal parenchymal echo, right kidney cyst, etc. With clinical exome sequencing, a novel heterozygous mutation c.679_680insA (p.R227Qfs*24) in PBX1 on chr1:164769105was identified. The diagnosis of CAKUTHED was made. Our literature review included 15publications. Including our case, 31 patients were reported. CAKUTHED could be characterized by kidney malformation, growth retardation, facial malformation, hearing abnormalities, skeletal malformation, reproductive malformation, heart malformation and so on. A total of 29 genetic variants were reported, including 15 mutations (repetition, insertion, substitution, deletion), 11 large fragment nucleotide deletion, and 3 exception exon deletion. Conclusion The clinical manifestations caused by PBX1mutations are complex and diverse. Exon sequencing can be used for precise diagnosis of CAKUTHED. Clinical manifestations are regularly followed up in multiple disciplines and symptomatic supportive treatment is given.PBX1 c. 679_680insA (p.R227Qfs*24) is a novel variant that haven’t been reported yet. Through the diagnosis and treatment of this child, the PBX1 related phenotype spectrum is broadened, and at the same time, growth hormone therapy for short stature caused by this gene mutation provides supporting evidence.

关键字 Congenital anomalies of kidney and urinary tract syndrome with or without hearing loss, abnormal ears, or developmental delay (CAKUTHED)； PBX1； recombinant human growth hormone

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Correlation analysis of IHH polymorphism and rhGH efficacy in children with idiopathic short stature

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Objectives: By exploring the correlation between SNP polymorphism and ISS in children with ISS in this region, as well as the differences between different genotypes and efficacy of IHH gene polymorphism in children with ISS after treatment with rhGH, the study provided theoretical basis for clinical individualized treatment.Methods: According to the TaqSNP retrieval strategy, by referring to PubMed database and relevant literature, five SNP loci of IHH gene were selected, and TSNP typing was performed on the sequencing platform to analyze the distribution frequency of alleles and genotypes. In order to further analyze the relationship between the SNP loci with the change in the distribution frequency of the intermediate gene and genotype in children with ISS and the efficacy of rhGH.Results: Through analysis, it was concluded that ISS children with different IHH genotypes had different therapeutic responses to rhGH.Conclusions: In this study, potential targets that may be related to rhGH efficacy in children with ISS were screened from the perspective of molecular biology, helping to investigate the molecular mechanism of differences in rhGH reactivity in different children with ISS, and providing a basis for future research and development of new drugs or treatment methods.

关键字 ISS, SNP, IHH, rhGH

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Genetic Diagnosis of Three Patients with Coffin-Siris syndrome-like Phenotypes and Transcriptomic Findings

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Although the whole-exome sequencing(WES) technology has been widely used in clinical practice, there are still many rare diseases with syndromic and non-syndromic neurological manifestations cannot be clearly diagnosed. Coffin-Siris syndrome (CSS) is an extremely rare dominant genetic disease with unexplained mental retardation and /or development disorders, and is a single-gene genetic disease caused by multiple genes. According to the typical clinical phenotypes, we can make clinical diagnosis of CSS, and a clear genetic diagnosis must rely on the results of genetic technologies. Whole-genome sequencing(WGS) is a more promising genetic diagnosis technology for rare disease patients. In this study, three patients with CSS-like phenotypes who have negative WES/CMA results were recruited. We used WGS technology to sequence the peripheral blood of the three families and adopt different methods to analyze the WGS data. Combining clinical phenotypes and final genetic results, we demonstrated that the three patients were CSS patients with de novo ARID1B copy number variants (CNVs). In order to further explore the possible pathogenesis of CSS, we treated three CSS patients as the experimental group and two normal volunteers as control, and performed RNA sequencing (RNA-seq). RNA-seq identified a total of 184 differentially expression genes (DEGs)in three patients and control groups, in which 116 were up-regulated genes and 68 were down-regulated genes. Functional annotation of DEGs showed that several biological processes (immune response, chemokine activity) and signaling pathways (cytokine-cytokine receptor interaction, chemokine activity) were highlighted. We speculated that ARID1B mutation may be a key trigger of immune response, which could be one of the possible mechanisms of the pathogenesis of CSS. Future studies are needed to determine the detailed mechanism of CSS. It is the first systematic study about CSS patients with de novo ARID1B CNVs, including genetic diagnosis and possible mechanisms analysis. Our research provided further support for WGS application for CSS-like patients with negative WES/CMA results and found underlying mechanisms and possible therapeutic targets of CSS.

关键字 Coffin-Siris syndrome, Genetic Diagnosis, Copy number variants, RNA-seq

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Investigation of Genetic Spectrum and Genotype-Phenotype Correlations in a Large Cohort of Chinese Patients with Mucopolysaccharidosis IVA

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Background Mucopolysaccharidosis IVA (MPS IVA) is a rare autosomal recessive disorder resulting from pathogenic variants of the N-acetylgalactosamine-6-sulfate sulfatase (GALNS) gene. Systematic analysis for genotype–phenotype correlations is essential due to hundreds of variants with various clinical effects.
Methods To establish the spectrum of GALNS variants and elucidate genotype-phenotype correlations, clinical form and molecular analysis were performed in 108 unrelated Chinese MPS IVA patients (82 severe, 14 intermediate, and 12 attenuated).
Results One hundred and one variants, including five complex variants, were identified, of which 47 were novel. Eighty-one percent (57/70) of severe patients with two identified alleles had at least one severe variant (33/57), or two missense variants that mapped to buried residues (24/57). At least one missense variant that mapped to surface residues was identified in the intermediate (78%, 7/9) and attenuated patients (86%; 6/7) with two identified missense variants. Additionally, the variants p.D388N and p.D60E showed an attenuated phenotype; the common variants p.M318R, p.P125L, and p.G340D were correlated with a severe type; p.X523E correlated with an attenuated type; and p.Y240C correlated with an intermediate type.
Conclusion Our study expanded genetics spectrum of GALNS variants and developed a flowchart to predict the phenotype of patients with MPS IVA.

关键字 Mucopolysaccharidosis IVA; MPS IVA; GALNS; variants; genotype¬–phenotype

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Effects and mechanisms of different types of maternal obesity on glucose and lipid metabolism in neonatal offspring

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Background: Maternal obesity include pre-pregnancy obesity (PO) and excessive gestational weight gain (EGWG). As the most important factors associated with perinatal outcomes, PO and EGWG have a profound impact on offspring health. Studies have shown that maternal obesity has different programming effects on offspring's physiological and organ development in different developmental Windows. We conducted this study to analyze the different effects of PO, EGWG, PO+EGWG on glucose and lipid metabolism in neonatal offspring, and to explore the possible mechanisms.
Methods: Animal models of PO, EGWG and PO+EGWG were established by feeding SD rats with high-fat diets at different periods. The control group had a normal diet before and during pregnancy, the PO group had a high-fat diet before pregnancy and a normal diet during pregnancy, the EGWG group had a normal diet before pregnancy and a high-fat diet during pregnancy, and the PO+EGWG group had a high-fat diet before and during pregnancy. The body weight of maternal rats before and during pregnancy and the birth weight of neonatal rats were recorded. Male neonatal rats were selected, fasting blood glucose levels were detected by glucometer, fasting insulin levels were detected by ELISA kit, hepatic triglyceride (TG) and cholesterol (TC) levels were detected by GPO-PAP enzyme method, hepatic lipid deposition were observed by HE staining and oil red O staining. The mRNA levels of hepatic key genes in glucose metabolism pathway IR, IRS, AKT and lipid metabolism FASN, SREBP1c, PPARα were detected by RT-PCR.
Results: The pre-pregnancy weight of maternal rats in high-fat diet group before pregnancy (PO group and PO+EGWG group) were significantly higher than those in normal diet group (control group and EGWG group); The percentage of weight gain during pregnancy of maternal rats in high-fat diet group during pregnancy (EGWG group and PO+EGWG group) were significantly higher than those in normal diet group (control group and PO group) ($P<0.05$). The birth weight of neonatal rats in PO group, EGWG group and PO+EGWG group were significantly higher than that in control group ($P<0.05$), and the birth weight of neonatal rats in PO+EGWG group was the largest. In terms of glucose metabolism, the levels of fasting blood glucose, insulin and HOMA-IR indexes in PO group, EGWG group and PO+EGWG group showed an upward trend than those in control group, though the difference was not statistically significant. The mRNA levels of IR, IRS and AKT in PO group, EGWG group and PO+EGWG group showed a downward trend than those in control group. In terms of lipid metabolism, the hepatic TG and TC levels in EGWG group and PO+EGWG group were significantly higher than those in control group, and hepatic lipid deposition was aggravated. The mRNA levels of FASN and SREBP1c in EGWG group and PO+EGWG group were higher than those in control group. The mRNA level of PPARα in PO+EGWG group was significantly higher than those in control group and PO group ($P<0.05$).
Conclusions: Animal models of PO, EGWG and PO+EGWG were successfully constructed by feeding SD rats with high-fat diets before pregnancy, during pregnancy, before and during pregnancy. PO+EGWG had the most significant effects on the birth weight and glucose and lipid metabolism in neonatal offspring. Compared with EGWG, PO had a relatively significant effect on glucose metabolism in neonatal offspring. And

compared with PO, EGWG had a relatively significant effect on lipid metabolism in neonatal offspring. The effects of maternal obesity on glucose and lipid metabolism in neonatal offspring were considered to be related to the expression changes of genes in glucose and lipid metabolism.

关键字 Maternal obesity; Neonatal offspring; Glucose and lipid metabolism; Rat

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Curcumin alleviates hepatic steatosis by improving mitochondrial function in postnatal overfed rats and fatty LO2 cells through SIRT3 pathway

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Background: Postnatal overfeeding could change hepatic metabolism and increase the risk of non-alcoholic fatty liver disease (NAFLD) in adulthood. Curcumin (CUR) is a polyphenol compound with lipid-lowering, antioxidative and liver protective activities. This study investigated the effects of CUR on hepatic steatosis in postnatal overfed rats and elucidated potential mechanisms in mitochondrial functions.
Methods: In vivo, male rats were adjusted to ten (normal litter, NL) or three (small litter, SL) at postnatal day 3. After weaning, NL rats were fed a normal diet (NL) or a high-fat diet (NH) for 10 weeks. SL rats were fed a normal diet (SL), a high-fat diet (SH), a normal diet supplemented with 2% CUR (SL-CUR) or a high-fat diet supplemented with 2% CUR (SH-CUR). In vitro, LO2 cells were stimulated with free fatty acids (FFA) for 24 h to induce the vitro model of NAFLD, then, CUR was given to the fatty LO2 cells for another 24 h. Histopathology, mitochondrial function, expression of lipid metabolism, mitochondrial antioxidative and biogenesis genes were assessed. The mechanisms of CUR on mitochondrial functions and hepatocyte lipid levels were discussed by siRNA.
Results: At week 13, compared with NL rats, SL and NH rats showed increased weight and hepatic lipid accumulation, and these changes were more obvious in SH rats ($P<0.05$). In addition, SL rearing upregulated mRNA levels of hepatic lipogenesis genes (acetyl-CoA carboxylase, sterol regulatory element binding protein-1c), and decreased mitochondrial DNA (mtDNA), superoxide dismutase (SOD) and glutathione peroxidase activity, and downregulated mRNA levels of mitochondrial b-oxidation (carnitine palmitoyltransferase 1, peroxisome proliferator-activated receptor , antioxidation (superoxide dismutase 2, nuclear factor E2-related factor 2), biogenesis (mitochondrial transcription factor A, nuclear respiratory factor 1, peroxisome proliferator-activated receptor coactivator -1) genes expression and protein level of Sirtuin 3 (SIRT3) compared with NL rats ($P<0.05$). The opposite trends were observed in SL-CUR and SH-CUR rats. In vitro, CUR decreased the levels of cellular lipids and mitochondrial reactive oxygen species, and increased mtDNA, ATP levels and SOD activity in fatty LO2 cells treated with FFA ($P<0.05$). However, these effects were blocked after SIRT3 silencing.
Conclusion: Postnatal overfeeding led to obesity, hepatic lipid accumulation and mitochondrial dysfunction including decreased antioxidant response and biogenesis in adulthood, and these outcomes were exacerbated by a postweaning high-fat diet. However, CUR supplementation alleviated hepatic steatosis, at least partially, by enhancing mitochondrial function through SIRT3. CUR may become a promising therapeutic agent for the prevention and treatment of NAFLD, especially in childhood and adolescence.

关键字 Curcumin; Non-alcoholic fatty liver disease; Postnatal overfeeding; Mitochondria; SIRT3.

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Case Report：17β-hydroxysteroid Dehydrogenase 10 Deficiency and Literature Review

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Objective To investigate the clinical characteristics and genetic analysis of 17β-hydroxysteroid dehydrogenase 10 (HSD17B10) deficiency, and so to improve the understanding of this disease. Method The clinical data of a male patient with HSD17B10 deficiency who was diagnosed and treated in the neonatal department of West China Second University Hospital of Sichuan University were analyzed. Literature was searched in the CNKI, VIP Database, and WanFang Database with "17β-hydroxysteroid dehydrogenase", "17β-HSD", "17β-hydroxyl Steroid dehydrogenase 10", "HSD17B10", "2-methyl 3-hydroxybutyryl-CoA dehydrogenase", "2-methyl 3-hydroxybutyryl-CoA dehydrogenase deficiency", "MHBD", "MHBDD" as keywords, and in PUBMED with "17β-hydroxysteroid dehydrogenase type 10 disease", "HSD10", "HSD17B10" and "2-methyl 3-hydroxybutyryl-CoA dehydrogenase deficiency", "2M3HBDD", "MHBD", and "MHBDD" as keywords. The data of patients with HSD17B10/2M3HBDD deficiency was reviewed from January 2020 to February 2021, and the clinical characteristics and the gene mutations of HSD17B10 deficiency were analyzed. Result The male newborn admitted to our hospital had poor response as the first clinical symptom, accompanied by severe metabolic acidosis, myocardial damage, and hyperammonemia, and died after giving up treatment. Genetic tests indicated mutation occur in HSD17B10 exon 6. c.740A>G (P.N247S). A total of 41 cases, including this case, with 16 different types of gene mutations in 38 papers were analyzed. Male patients (n=38, 92.7%) were significantly more than female, and the sickness was more serious than that of female. Most patients had neurological abnormalities (n=37, 90.2%), which might be accompanied with metabolic acidosis (n=13, 31.7%), hypoglycemia (n=8, 19.5%), retinopathy (n=7, 17.1%),cardiomyopathy (n=6, 14.6%) and nystagmus (n=4, 9.8%). The neonatal type of disease usually presented severe metabolic acidosis, the younger the age at the time of onset, the higher the mortality and the worse the prognosis. This disease can be diagnosed by HSD17B10 gene mutation analysis. Conclusion There are different types of HSD17B10 deficiency gene mutations, and thus different severity of the disease. The clinical characteristics of male children is severe and the prognosis is poor. There is still no effective treatments to date. If there were a family history of this disease, early prenatal consultation and prenatal diagnosis should be required.

关键字 17β-hydroxysteroid dehydrogenase 10 deficiency; newborns; inherited metabolic diseases; mitochondrial diseases

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Treatment of congenital adrenal hyperplasia and Klinefelter Syndrome with central precocious puberty

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Background: The simultaneous occurrence of Klinefelter syndrome (KS) and congenital adrenal hyperplasia (CAH) is extremely rare, as the first causes androgen deficiency, while the latter results in androgen excess.
Case report: We present the 7th reported case of the simultaneous KS and CAH in a boy with central precocious puberty (CPP) due to protopathy caused by CAH. He presented with increased gonadotropin and excessive androgen levels, and was diagnosed with KS due to his unexpected karyotype analysis results. This is the first reported case of an association between KS and CAH to undergo gonadotropin-releasing hormone analog (GnRHa) and recombinant human growth hormone (rhGH) therapy to increase his predicted final height.
Conclusion: Although KS may cause hypogonadism, the patient should be administered GnRHa and rhGH therapy if simultaneous CAH, CPP, and KS are present to increase the patient’s predicted final height. Excessive androgen levels may mask the symptoms of KS-related hypogonadism during childhood; however, the patient should be made aware of the possibility of hypogonadism developing in the future.

关键字 congenital adrenal hyperplasia，Klinefelter syndrome，gonadotropin-releasing hormone analog

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Associations between exposure to a mixture of phenols, parabens, and phthalates and sex steroid hormones in children 6 - 19 years from NHANES, 2013 - 2016

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Background: Humans are typically exposed to mixtures of environmental endocrine-disrupting chemicals (EDCs) simultaneously. However, most studies regarding environmental chemicals and sex hormones have considered only a single chemical or a group of similar chemicals instead of chemical mixture exposures.
Objectives: To examine the effect of exposure to mixtures of 7 chemicals, including 2 phenols [bisphenol A (BPA) and bisphenol S (BPS)], 2 parabens [methylparaben (MeP) and propyl paraben (PrP)], and 3 phthalate metabolites [Mono-benzyl phthalate (MBZP), mono-isobutyl phthalate (MIBP), mono (carboxyoctyl) phthalate (MCOP)] on sex steroid hormones.
Methods: Data came from the U.S. National Health and Nutrition Examination Survey (NHANES) 2013 - 2016. A total of 1,179 children aged 6 - 19 years who had complete data on both 7 chemicals and sex steroid hormones of estradiol (E2), total testosterone (TT), and sex hormone-binding globulin (SHBG) were analyzed in this cross-sectional study. Free androgen index (FAI) calculated as TT divided by SHBG and a ratio of TT to E2 (TT/E2) were generated. Puberty was defined if TT ≥ 50 ng/dL in males, E2 ≥ 20 pg/ml in females; otherwise prepuberty was defined. Linear regression, weighted quantile sum (WQS) regression, and Bayesian kernel machine regression (BKMR) were performed to estimate the associations of individual chemical or chemical mixtures with sex hormones. We further assessed the heterogeneity of those associations by stratification of age-gender and puberty-gender status.
Results: The linear regression showed that 2 phenols, 2 parabens, and 3 phthalate metabolites were generally negatively associated with E2, TT, FAI, and TT/E2, while positively with SHBG. Moreover, the associations were more pronounced in pubertal than prepubertal children. The aforementioned associations were confirmed when applying WQS regression. The WQS index was negatively associated with E2 and FAI among both pubertal boys and girls in which MBZP (weighted 0.39), MIBP (0.39), and MCOP (0.32) had relatively high weights, while positively with SHBG among pubertal girls in which MeP (0.48) was the most heavily weighing chemical. The BKMR analyses further identified that the overall effect of chemical mixtures was negatively associated with TT and FAI, while positively with SHBG in particular among pubertal children, and MBZP [posterior inclusion probability (PIP) 0.84 - 1.00] contributing most in the models.
Conclusions: Exposure to phenols, parabens, and phthalates, either individuals or as a mixture, was generally negative associated with E2, TT, FAI and TT/E2, but positively with SHBG. Those associations were stronger among pubertal children. Phthalates metabolites were the most highly weighted chemicals. Given the cross-sectional nature of the analysis, prospective cohort studies are warranted to confirm the findings.

关键字 Chemical mixtures; Sex steroid hormones; Weighted quantile sum regression; Bayesian kernel machine regression

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Genetic and Phenotypic Characteristics of 107 Patients with Mucopolysaccharidosis Type II: A Retrospective Observational Study in China

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Background: Mucopolysaccharidosis Type II (MPS II) is a rare, progressive and ultimately fatal X-linked lysosomal storage disorder caused by mutations in the iduronate-2-sulfatase (IDS) gene. MPS II has a relatively high prevalence in Eastern Asian countries but there are few reports on patients in China. This report represents one of the largest studies of MPS II and is based on a retrospective, single-center analysis of medical records between 2008 and 2020. Data analyses were descriptive.
Methods and Results: A total of 107 patients (all male) were enrolled, including 11 with a family history of MPS II. Of 40 patients with gene sequencing data, 33 unique IDS mutations were identified, including eight previously unreported mutations. Mean age at diagnosis was 5 years (range: 2 months to 22 years) and onset of MPS II symptoms was predominantly recorded between 2 and 6 years of age. Musculoskeletal and dermatologic abnormalities were the most common clinical manifestations. Treatment was generally supportive and palliative with 38 patients undergoing ⩾1 surgical treatment. One patient underwent a bone marrow stem cell transplant. Morbidity and mortality: Two patients, aged 11 years and 15 years, respectively, were wheelchair-bound and one 11-year-old was unable to eat independently. Three patients are now known to have died, aged 10, 11 and 13 years, respectively.
Conclusions: This study re-emphasized the clinical value as one of the largest analyses of an MPS II population and briefly summarize the key findings. It noted that the importance of early MPS II diagnosis and the importance of early initiation of enzyme replacement therapy to maximize clinical benefit.

关键字 Mucopolysaccharidosis Type II，Genetic and Phenotypic Characteristics

分类：9. Endocrinology 内分泌遗传代谢
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Clinical significance of GnRH pulse pump in Adolescent boys with Congenital Hypogonadotropic Hypogonadism

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The purpose of this study is to investigate the clinical application of short-term GnRH pump subcutaneous pulse infusion in the differential diagnosis of children with CHH and CDGP and the effectiveness of CHH treatment. Methods: A retrospective study was conducted on 26 children with delayed puberty diagnosed in the pediatric endocrinology clinic and ward of Shanghai Children's Hospital from 2016 to 2020, including CHH group (n=20) and CDGP group (n=6). The characteristics of puberty in CHH and CDGP group were evaluated before treatment. Both groups were treated with GnRH pump subcutaneous pulse for one week and some children with CHH (n=5) were treated for 3 months. Routine GnRH challenge test was performed one day before treatment and the next day after treatment. The changes of LH, FSH, testosterone and testicular volume were observed before and after treatment. Results: There were no significant differences in age, height, BMI, testis size, peak value of GnRH, LH and FSH between CHH group and CDGP Group (P<0.05) , but significant differences in the testosterone level after HCG (P= 0.044); After one week of GnRH pump treatment, the basal and peak values of LH and FSH, the testosterone level in CHH group were significantly higher than those before treatment(P<0.05), but still lower than those in CDGP group, while the peak values of LH, the basal and peak values of FSH in CDGP group were significantly higher(P<0.05), however there were no significant abnormalities in testosterone level and testicular volume(P>0.05). Among these two groups, there were no significant abnormalities in the peak values of LH, the basal and peak values of FSH, testosterone level and testicular volume before and after treatment GnRH pump, except that the LH base value of CHH was significantly lower than CDGP(P<0.05). After 3 months of treatment with GnRH pump in CHH group, the peak values of LH and FSH were significantly improved(P=0.017,0.015), but the testosterone level and testicular volume were not significant improved. Mutations were detected in 14 out of 20 CHH patients, mostly in FGFR1 gene (n=7) and ANOS1 gene (n=4), there were no significant differences in the base values of LH, FSH, testosterone, and the peak values of LH, FSH and testosterone after using GnRH pump for one week (P>0.05). Conclusion: One week treatment with GnRH pump is helpful to differentiate CHH from pituitary diseases, combined with HCG stimulation test and gene detection is helpful to early distinguish CHH from CDGP. Short-term treatment with GnRH pump for 3 months can significantly improve the levels of LH, FSH, testosterone and testicular volume, which is conducive to the follow-up gonadotropin replacement therapy. There is no significant correlation between the curative effect of short-term GnRH pump and their genotypes. How to choose the treatment regimen of GnRH pump, HCG and HCG/HMG is beneficial to maintain the function of gonads in adolescents, and further prospective clinical research is needed.

关键字 Gonadotropin releasing hormone pump; Congenital hypogonadotropic hypogonadism; Constitutional delay of growth and puberty; Adolescent

分类：9. Endocrinology 内分泌遗传代谢
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Transcriptome-scale spatial gene expression in rat arcuate nucleus during puberty

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Background: Adolescent sexual maturation is an important part of an individual ontogeny in mammalian development. The active and high hormone levels in this juvenile period promote the fertility attainment, body growth, increased metabolism and acceleration of psychological development. The initiation of puberty is attributed to the increased gonadotropin-releasing hormone (GnRH) secretion in pulsatile manner and the subsequent activation of hypothalamic-pituitary-gonadal axis. A variety of neurons in hypothalamus undergo a complicated regulation on transcription activity of multiple genes for hypothalamic-pituitary-gonadal axis activation during pubertal development. Identification of puberty-associated cell composition and characterization of the unique transcriptional signatures across different cells are beneficial to specific neurons isolation and advanced understanding their functions.
Methods: The whole brain of female Sprague-Dawley rats in postnatal day-25, 35 and 45 were harvested and performed 10 μm serial tissue sections transversely to expose arcuate (ARC) nucleus (bregma: -2.52 to 2.92 mm, interaural: 6.08 to 6.48 mm) and processed the spatial transcriptomics sequencing for the dynamic spatial atlas of gene expression in the ARC by 10x Genomics Visium platform. Flow cytometric assay were conducted to isolate alive Kiss1 neurons by the candidate surface membrane biomarkers Slc18a3.
Results: The t-distributed stochastic neighbor embedding (t-SNE) dimension reduction clustering analysis characterized fourteen cell clusters in whole brain, and four sub-clusters in ARC. Highly expressed Tgfbi, Nr5a2, Spp1, Galp, Fndc3c1, Slc18a3, Dlx5, Glp1r, Tekt3, and Kiss1 were considered as the appropriated candidate hallmarks to distinguish the largest number of Kiss1 positive neurons in Sub-cluster 1 from other three sub-clusters. Furthermore, the unsupervised pseudotime analysis showed that the overall transcriptome of a proportion of ARC neurons in PND-35 were different from in PND-45, indicating two parallel developmental routes of ARC neurons from PND-25 to PND-35 as well as from PND-25 to PND-45, but not a one-way route from PND-25, PND-35 to PND-45. Moreover, three modules with the distinct expression landscape of 2,948 hypervariable genes in each module were characterized along the puberty process based on the gene expression tendency. Genes in Module 1 contributed to enhancing glial cells but repressing neuron cells proliferation induced by estradiol, genes in Module 2 substantially played a regulatory role in hormone secretion, and genes in Module 3 were responsible for neurons differentiation and signals transmission, indicating that multiple genes in ARC participated in pubertal onset and development actually via distinct functions.
Conclusion: Our data revealed a comprehensive transcriptomic overview of ARC with different pubertal stages, which could serve as a valuable resource for puberty and sexual development disorders study. We also provide a method to precisely capture Kiss1 neurons from wild type rodents.

关键字 Puberty, hypothalamus, spatial transcriptome, ARC, Kiss-1, Slc18a3

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Growth hormone treatment in children with Perthes disease and growth hormone deficiency: a case report and literature review

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Objective To explore the efficacy and safety of recombinant human growth hormone (rhGH) in Perthes disease with growth hormone deficiency (GHD) in a child.
Method The clinical data of Perthes disease with GHD in a child treated with rhGH for 4 years were retrospectively analyzed.
Results Here we reported a 11.9-year-old boy, who developed the right hip joint pain at the age of 2.7, and was diagnosed with "Perthes disease", which is the osteonecrosis of the femoral head. He underwent surgery at the age of 4.8-year-old and recovered well including pain reduction and function of the hip joint recovery. At the age of 6.7-year-old, he was diagnosed with complete growth hormone deficiency. Physical examination noted significantly short stature with low height 108.8cm (<3rd, -2.45SD), growth rate <5 cm/year. Hormone analysis revealed low insulin-like growth factor-1 (IGF-1) 72.7 ng/mL (-2SD～-1SD), low insulin-like growth factor binding protein-3 (IGFBP-3) 2280ng/mL (<-2SD), and growth hormone stimulation test displayed GH peak value was 1.54ng/ml. His bone age was 4.5-year-old, more than 2 years behind the chronological age. After evaluating the skeletal development status and excluding contraindications, the child was given low-dose rhGH by subcutaneous injection once daily, which the initial dose of rhGH was 0.105IU·kg-1·d-1. Treatment started from the age of 7.9-year-old, with the height of 115.8cm (<3rd, -2.6SD), the weight of 31.5kg, and the testicular volume of 1~2ml. rhGH treatment last for 4 years till he is 11.9 years old , with the dose of rhGH 0.062～0.112IU·kg-1·d-1. His height is 152.3cm (50 ~ 75th centile, + 0.29SD), weight 64.5kg, testicular volume 10ml now. During the treatment of rhGH, the growth rate was significantly improved and no adverse reactions were caused. Throughout the first year of treatment, the growth rate was 9.7 cm per year, and in the next three years it was 10.7 cm per year, 5.3cm per year and 10.8 cm per year, respectively. He had an annual growth rate of approximately 9.1cm per year, compared to less than 5 cm per year before growth hormone therapy. As the child underwent the surgical treatment for femoral head necrosis, lack of physical exercise led to the obesity. Nevertheless, regular monitoring of fasting glucose and insulin levels fluctuated within the normal range, and there was no signs of insulin resistance such as acanthosis nigricans. Levels of IGF-1 and IGFBP3 gradually increased over the 4-year treatment period, in sync with age and adolescence. The indexes of liver and kidney function and thyroid function were within the normal range. The bone age increased year by year, but there was no significant acceleration of progress, and it is now basically in line with age. The X-ray of the hip joint was not abnormal.
Conclusions The rhGH treatment can improve the height of children with Perthes disease and growth hormone deficiency without causing adverse reactions such as osteonecrosis of femoral head, which shows good clinical efficacy and safety.

关键字 short stature; Perthes disease; growth hormone deficiency; recombinant human growth hormone

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Origin of the X-chromosome influences the development and treatment outcomes of Turner syndrome

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Turner syndrome (TS) affects 1/2500 live-born female infants. In the present study, we attempted to clarify the relationship between genetic factors (especially the X-chromosome origin), clinical features, body/sexual development, and treatment outcomes. We enrolled 39 female infants aged between 3 and 14 years. General demographic and clinical features were documented, and laboratory analysis of blood samples was performed. Subject karyotype was determined by G-banding of 50 peripheral white blood cells, and the parenteral origin of the retained X-chromosome was determined. Next, growth hormone (GH) treatment was prescribed for 12 months, with follow-ups performed as determined. For patient groups separated according to X-chromosome origin, the basal height, bone age, insulin-like growth factor (IGF)-1, and insulin-like growth factor binding protein-3 (IGFBP-3) levels were comparable; however, after the 12-month treatment, significant differences in the height increase and IGF-1 levels were observed. If the X-chromosome (or chromosomes) originated from both parents, the increase in height was less substantial, with lower serum IGF-1 levels. The uterine size, prolactin level, increased weight after treatment, and bone age difference after treatment negatively correlated with the mother's age at the time of birth. The mother's height at the time of birth demonstrated a negative correlation with the basal bone age difference and a positive correlation with the IGF-1 level. In summary, the retained X-chromosome derived from both parents is associated with poorer response to GH therapy. The mother’s age and height at the time of birth can strongly impact the patient’s body/sexual development and the response to GH treatment. Thus, the mother’s age and height at the time of birth and the parental origin of the X-chromosome should be carefully considered before developing a treatment plan for TS.

关键字 Keywords: Turner syndrome, X-chromosome origin, IGF-1.

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Adoptive transfer of HO-1 high expression imDC delays the onset of T1DM in NOD mice

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Adoptive transfer of HO-1 high expression imDC delays the onset of T1DM in NOD mice
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Objective: Immature dendritic cells (imDC) induced in vitro have been found to play a crucial part in the inhibition of graft rejection. Immature dendritic cells were induced to overexpression Heme oxygenase-1(HO-1), showing a better protective effect in mouse heart transplantation model. However, it is still unclear whether high expression of HO-1 in imDC also has a protective effect on autoimmune diabetes. Therefore, we investigate whether imDC with high expression of HO-1 could delay the occurrence of type 1 diabetes mellitus in NOD mice.
Methods: Murine bone marrow-derived dendritic cells were induced with rGM-CSF and rIL-4 in vitro. Suspended cells stimulated by LPS were used as mature dendritic cells (mDC). Adherent cells were used as imDC induced with CoPP (HO-1 inducer) or SnPP (negative control). Detected the expression level of costimulatory molecules on DC surface and intracellular HO-1.
NOD mices (6 weeks old) were divided into four groups: control group and three treatment groups treated with imDC, CoPP-induced imDC or SnPP-induced imDC. Saline or 2×106 cells with different treatment were injected into mice at 8 and 10 weeks old. Blood glucose was monitored once a week from 8 weeks of age until the onset of diabetes or the end of the study (20 weeks of age). At the end of study, the incidence of diabetes, the degree of islet inflammation, the area of insulin-secreting pancreatic β cells and serum insulin level in each group were compared.
Results: Compared with imDC, the mean fluorescence intensity (MFI) of co-stimulatory molecules CD80 and CD40 on the surface of cells with CoPP treatment was reduced ($P<0.05$), the expression level of HO-1 protein in cells with CoPP treatment was significantly increased ($P<0.05$).
In vivo, compared with the control group, the incidence of T1DM in the CoPP group was significantly reduced (30.8% VS control group: 61.5%, $P<0.05$), the insulitis score was also deceased ($P<0.05$). The differences in serum insulin level, body weight and the remaining islet β cell area among all groups were not significant.
Conclusion: CoPP-induced imDC with high expression of HO-1 have a stronger ability to inhibit immune response and reduce the incidence of diabetes in NOD mice, which may become a new treatment strategy for type 1 diabetes mellitus.

关键字 Type 1 diabetes mellitus; dendritic cell; immature dendritic cell; heme oxygenase-1; immunoregulation; non-obese diabetic mice

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Clinical changes of leptin/ghrelin and PAI-1 levels in adolescent girls with dysfunctional uterine bleeding

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Objective: The objective is to observe the expression of leptin, ghrelin and PAI-1in adolescent girls with dysfunctional uterine bleeding (DUB).
Methods: This was a prospective study. A total 80 adolescent girls were enrolled. There were 2 groups, including 60 girls with DUB and 20 healthy girls, respectively. Peripheral venous blood samples were obtained aseptically from the girls between 8 AM and 10 AM after at least 8 hours fasting on the 5th -7th day of menstruation, and successively centrifuged at 2000 rpm for 10 mins. The concentration of leptin, ghrelin, PAI-1 and sex hormones in peripheral blood were detected.
Results: The results showed that the level of leptin and PAI-1 in girls with DUB were significantly lower than that in healthy girls ($p< 0.01$), and the level of ghrelin was significantly higher than that in healthy girls ($p < 0.05$). At the same time, we also found that there was a negative correlation between the level of leptin, ghrelin and estradiol in girls with DUB.
Conclusion: In this study, we found that the expression level of leptin in peripheral blood of DUB girls was significantly lower than that of the normal control group, while the expression level of ghrelin was higher than that of the normal control group, and that girls with DUB showed negative correlation between the level of leptin, ghrelin and estradiol, suggesting that the abnormal expression of leptin / ghrelin, related factors of energy metabolism, may affect the HPO axis of adolescent girls and lead to the occurrence of dysfunctional uterine bleeding; At the same time, the level of PAI-1 in peripheral blood of DUB patients is significantly lower than that of normal control group, which may affect the contractile function of endometrial vessels and may be one of the causes of endless menstruation.

关键字 leptin； ghrelin；dysfunctional uterine bleeding in adolescent girls；PAI-1; energy metabolism

分类：9. Endocrinology 内分泌遗传代谢
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A low abundance of genus Bacteroides in gut microbiota is negatively correlated with blood phenylalanine levels in Uygur patients with phenylketonuria

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Background: A low-phenylalanine (Phe) diet affects the metabolism and diversity of gut microbial communities in children with phenylketonuria (PKU). Our study examined gut microbiota characteristics and metabolic pathways, and their correlations with clinical phenotypes in a high-incidence population. Method: We assessed clinical phenotypes and gut microbiota by 16S ribosomal RNA (rRNA) sequencing, and performed a correlation analysis between phenotype and gut microbiota in a PKU group (n=11) and a healthy group (n=11). Result: The PKU group had significantly lower microbiota diversity than the healthy group (Pshannon=0.014). Phylum-level composition differed significantly between the PKU and healthy groups (Firmicutes: 44.3% vs. 43.1%; Actinobacteria: 25.9% vs. 3.3%; Bacteroidetes: 16.6% vs. 53.2%; and Proteobacteria: 10.9% vs. 0.12%, respectively). Further, a significantly decreased level of genus Bacteroidetes (P<0.0001) in the PKU group was negatively correlated with blood Phe level (P=0.014). The microbial function prediction of the Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways exhibited a decreased ability of glycan degradation and glutamate metabolism in the PKU group. Conclusion: Our findings revealed that genus Bacteroide was not only in extremely low abundance in the PKU group, but was also negatively correlated with blood Phe level. The remarkable capability of genus Bacteroides to use complex recalcitrant glycans may be the main reason for the decreased ability of glycan degradation in the PKU group.

关键字 Phenylketonuria (PKU); gut microbiota; 16S ribosomal RNA sequencing (16S rRNA sequencing); clinical phenotype; Uygur

分类：9. Endocrinology 内分泌遗传代谢
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Clinical features of 123 patients with hyperinsulinemic hypoglycemia auxiliary diagnosed by 18F-DOPA-PET CT scanning

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Objective To summarize the clinical features and therapeutic outcomes of patients with hyperinsulinemic hypoglycemia (HH) auxiliary diagnosed by 18F-DOPA positron emission tomography (PET) CT scanning. Method The clinical data of 123 patients who were diagnosed with hyperinsulinemic hypoglycemia by comprehensive clinical diagnostic procedures in the Department of Pediatric Endocrinology and Inherited Metabolic Diseases, Children's Hospital of Fudan University between January 2016 and December 2020 were retrospectively analyzed. Clinical data such as gender, age of onset, province, concurrent serum insulin level measured during hypoglycemia, lesion type of pancreas by 18F-DOPA-PET CT scanning, genetic test results, and post-treatment response were collected successively. The clinical features and therapeutic outcomes were compared between patients with focal and diffuse pancreatic lesions. According to different data, t test, Rank sum test, and χ^2 test were used for comparison between groups. Result A total of 123 patients with hyperinsulinemic hypoglycemia (72 males and 51 females), whose onset age was 3 days (ranging from 1 day to 4860 days), were recruited from 24 provinces. The concurrent serum insulin level was 7.1mU/L (0.4-303mU/L) during hypoglycemia. 18F-DOPA-PET CT scanning showed focal lesions were 25% (31/123) and diffuse lesions were 74.8% (92/123). 64.2% (79/123) of the HH cases were found to have pathogenic gene variants, in which 88.6% (70/79) were found to have KATP channel related genes (61 harbored ABCC8 mutations, 9 harbored KCNJ11 mutations). The effective rate of diazoxide in diffuse lesion group was significantly higher than that in focal lesion group [28.3% (26/92) vs 9.7% (3/31), χ^2 =10.31, P = 0.001]. Thirty-seven patients (17 focal and 20 diffuse) received surgical treatment with a success rate of 67.6% (25/37). Conclusions 18F-DOPA-PET CT scan can improve the success rate of surgery. Comprehensive diagnosis of the etiology of hyperinsulinemic hypoglycemia by genetic analysis and 18F-DOPA-PET CT scanning can result better treatment and prognosis.

关键字 Hyperinsulinemia; Hypoglycemia; Positron-emission tomography

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35 cases of 46, XY Disordered Sex Development in SRD5A2 gene mutation analysis

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Objective: Analyze SRD5A2 gene mutations with Disordered Sex Development in 46,XY
Methods: We studied a series of 35 index patients with 46,XY DSD form January 2015 to January 2020 in our hospital. Form peripheral blood to extract genomic DNA, the gene was amplified by PCR and sequenced by Sanger sequencing method. All SRD5A2 gene coding sequence were detected, Application seqMan7.1, MutationSurveyor3.97 software to analyze the results of the sequencing.
Results: (1) SRD5A2 gene mutations were found in 11 cases (account for 31.4%) , （2）4 cases had compound mutations (p.G203S / p.R227Q), 7 patients had the single missense mutation(five cases with p.R227Q, one case with p.A228V, one cases with p.L20P). (3) 30 normal control’s、SRD5A2 gene sequence were sequenced. we did not find the mutations.
Conclusion: 1.46,XYDSD with male pseudohermaphroditism or Hypospadias should be preferred to sequence SRD5A2 gene.2.p.R227Q appears to be common in Chinese 5α-RD2 patients. 3.The relation of genotype and phenotype need to be further enlarge the sample for analysis.

关键字 46, XY,AR gene;,SRD5A2 gene, Hypospadias, Micropenis

分类：9. Endocrinology 内分泌遗传代谢
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Clinical severity prediction in children with osteogenesis imperfecta caused by COL1A1/2 defects

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Introduction: Ninety percent of Osteogenesis imperfecta (OI) cases are caused by pathogenic variants in the COL1A1/COL1A2 gene. The Sillence classification describes four OI types with variable clinical features ranging from mild symptoms to lethal and progressively deforming symptoms.
Methods: We established a prediction model of the clinical severity of OI based on the random forest model with a training set was obtained from the Human Gene Mutation Database, including 790 records of the COL1A1/COL1A2 genes. The features used in the prediction model were respectively based on variant type features only and the optimized features.
Results: With the training set, the prediction results showed that the area under the receiver operating characteristic curve (AUC) for predicting lethal to severe OI or mild to moderate OI were 0.767 and 0.902 respectively when using variant type features only and optimized features for COL1A1 defects, 0.545 and 0.731 respectively for COL1A2 defects. For the 17 patients from our hospital, prediction accuracy for the patient with the COL1A1 and COL1A2 defects were 76.5% (95%CI: 50.1%-93.2%) and 88.2% (95%CI: 63.6%-98.5%), respectively.
Conclusion: We established an OI severity prediction model depending on multiple features of the specific variants in COL1A1/2 genes, with a prediction accuracy of 76% - 88%. This prediction algorithm is a promising alternative that could prove to be valuable in clinical practice.

关键字 Osteogenesis imperfecta, COL1A1 gene, COL1A2 gene, clinical severity, prediction model

分类：9. Endocrinology 内分泌遗传代谢
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The association between new onset type 1 diabetes and gut microbiota perturbation caused by antibiotic and neonicotinoid exposure

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Objective: The real-world exposure levels of non-therapeutic antibiotic and neonicotinoid in type 1 diabetes (T1D) children and their potential associations as environmental triggers through gut microbiota shifts remained unknown. We thus investigated the characteristics of gut microbiota according to different antibiotics and neonicotinoids exposure levels and analysed their associations with T1D.
Methods: Fifty-one newly-onset T1D children along with sixty-seven age-matched healthy controls were recruited from eight cities in China between January 2019 to March 2020. Urine concentrations of twenty-eight antibiotics and eight neonicotinoids were measured by isotope dilution ultra-performance liquid chromatography coupled to quadrupole time-of-flight mass spectrometry. Urine antibiotics/neonicotinoids concentrations higher than the 50th percentile were regard as the high exposure group otherwise as the low exposure group. The 16S rRNA of fecal gut microbiota were sequenced and their correlation with urine antibiotics and neonicotinoids concentrations were analysed.
Results: The overall detection rates of antibiotics and neonicotinoids were 66.1% and 60.2%. The T1D group showed a higher neonicotinoid-detection rate ($p = 0.044$) than the control group. The T1D group displayed decreased richness and diversity of gut microbiota, a lower abundance of butyrate-producing genera and a higher abundance of opportunistic pathogens, relative to the control group. Different veterinary and veterinary/human antibiotics (VA+V/HA) or neonicotinoids exposure levels didn’t affect overall richness and diversity of gut microbiota, but caused a higher Bacteroidetes: Firmicutes ratio at phylum level, and a lower abundance of Ruminococcaceae and Lachnospiraceae at family level in the high exposure group. Children with high exposure of VA+V/HA and neonicotinoids had a lower abundance of Faecalibacterium, Ruminococcus 2 and Fusicatenibacter, relative to those with low exposure levels (Figure 1).
Conclusions: High VA+V/HA and neonicotinoids exposures caused changes in gut microbiota featured with lower abundance of butyrate-producing genera, which might increase the risk of T1D.

关键字 Type 1 diabetes mellitus, Neonicotinoids, Antibiotics, Gut microbiota

分类：9. Endocrinology 内分泌遗传代谢
1262

Clinical and gene mutation analysis in a patient with a noval PCSK1 mutation

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Background: Congenital deficiency of the neuroendocrine-specific enzyme prohormone convertase (PC) 1/3, caused by mutations in the PCSK1 gene, play a pivotal role in the activation of biologically inactive hormones, is characterized by severe congenital malabsorptive diarrhea, early-onset obesity, dysregulation of glucose homeostasis in humans, and certain endocrine abnormalities. To date, only few unrelated subjects with this disorder have been reported. Their pathophysiological mechanisms are largely unknown.
Method: We suspected PCSK1 deficiency in a new born boy cased on the presence of congenital diarrhea, reactive hypoglycemia, severe acidosis, electrolyte disturbance, and polyuria. Sequencing the whole coding region and splice sites.
Results: We detected a novel homozygous PCSK1 mutation, c.867_872delinsTGCTTTTGA (p.E289_G291delinsDAFD), in the patient. The father is heterozygous at the site, and the mother is normal. We characterized the clinical phenotype and gene mutation analysis of the PCSK1 of the patient.
Conclusions：This case extends the clinical phenotype and molecular spectrum of human congenital PCSK1 deficiency.

关键字 PCSK1 基因突变，肥胖

分类：9. Endocrinology 内分泌遗传代谢
1281

The effect of long-term valproic acid therapy on lipid profile in pediatric patients with epilepsy: a meta-analysis

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Epilepsy is a chronic neurological problem of childhood which may require long-term period antiepileptic drugs (AEDs) therapy, in some patients continuing throughout their life. Valproic acid (VPA), as a broad spectrum anticonvulsant drug, is one of the most commonly administered AEDs for the treatment of childhood epilepsy. Beside its effectiveness, VPA has also been reported to be associated with metabolic and endocrine disorders as weight gain and hepatotoxicity that may limit its clinical application. However, the exact pathophysiologic pathways underlying the VPA-associated adverse drug reactions remain an unresolved conundrum. Moreover, it is suggested that VPA induced lipid disruption through inducing long-chain fatty acid uptake and triglycerides (TG) synthesis in vivo. However, the effects of VPA on changes in lipid profiles in clinical remain controversial. Since the long-term effects of medication with VPA during childhood and adolescence on lipid metabolism are still contradictory and there is no meta-analysis on this topic, we decided to do a meta-analysis to evaluate the effects of VPA treatment on lipid profile in children and to answer the question “whether VPA treatment influence blood lipids or not.

Relevant papers were searched in PubMed, Web of science, Cochrane Library and Embase database. The following Medical Subjects and Headings (MeSH) terms and keywords were used: 1) Valproic acid; 2) “cholesterol” or “triglycerides” or “low density lipoprotein cholesterol” or “high density lipoprotein cholesterol”. The data were extracted from each relevant paper: first author’s information and publication year, sample size, intervention dosage, study duration, age, sex, and results. Means and standard deviations (SD) of the main outcomes (TC, LDL-C, HDL-C, and TG) were also extracted for the effect size calculation. The analysis was performed using the Cochrane Collaboration’s Review Manager Software (RevMan, version 5.4). We used the mean difference as the effect indicator and gave each effect size point estimate and 95% CI. Q test and I2 statistics are used to perform the heterogeneity tests.

Initially, 2494 citations were identified, and 1219 abstracts were screened after duplicates were removed. After screening titles/abstracts, 26 full-text articles were retrieved and re-assessed for eligibility. Eleven articles were excluded after full-text screening: 2 studies with insufficient data, and 9 studies with no control group. Finally, 15 studies met the inclusion criteria and were included in this meta-analysis. These studies all included a control group consisting of sex and age matched healthy children. The duration of valproate treatment was more than three months in all the studies including years of valproate therapy in some reports. The results showed that VPA monotherapy significantly decreases the TC level [MD=-6.34, 95%CI (-12.30, -0.37), P=0.04] and VPA therapy causes a significant decrease in LDL level [MD=-7.75, 95%CI (-13.48, -2.02), P=0.008]. But no significant difference in HDL level was found between the two groups [MD=0.21, 95%CI (-2.73, 3.16), P=0.89] and there was no statistical difference in TG between VPA therapy group and control group [MD=0.21, 95%CI (-2.65, 3.06), P=0.89]. The results showed that VPA therapy was associated with a significant reduction in TC level [MD=-6.34, 95%CI (-12.30, -0.37), P=0.04]. Also, VPA therapy was associated with a significant decrease in LDL-C levels

[MD=-7.75, 95%CI (-13.48, -2.02), P=0.008]. No significant effect was observed in HDL-C and TG.
In conclusion, this meta-analysis showed that pediatric patients receiving VPA treatment had lower TC and LDL-C levels. In long-term therapy, epileptic children should carefully be monitored in terms of lipid profiles which are related to metabolic syndrome.

关键字 Valproic acid, TC, LDL-C, HDL-C, TG

分类：9. Endocrinology 内分泌遗传代谢
1329

The value of Kisspeptin for predicting the initiation of puberty

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Objective: The aim of this study is to investigate the value of kisspeptin for predicting the initiation of puberty from clinical application perspective when Gonadotropin Releasing Hormone (GnRH) provocation test cannot be performed.
Materials and method: The girls with the chief complaint of development of secondary sexual characteristics were recruited. Physical examination, laboratory tests and image examination were given, Peripheral blood 3~4 ml were collected. The levels of kisspeptin were measured using Enzyme Linked Immunosorbent Assay (ELISA) Kit. The Receiver Operating Characteristic (ROC) curve was used to determine the value of Kisspeptin in identifying the initiation of Hypothalamic-pituitary-gonadal axis (HPGA).
Results: The levels of kisspeptin in HPGA-activated group(including central precocious puberty and rapidly progressive puberty) was statistically higher than the levels of Premature thelarche(PT) group(P<0.05). The results of Spearman correlation showed that the level of Kisspeptin was positively correlated with many clinical indicators, especially the peak LH and the ratio of peak LH/FSH. The Area under curve(AUC) of Kisspeptin were 0.702, and when the level of kisspeptin was 310.38pg/ml, the Youden index got the largest (0.418), the sensitivity and specificity was 81.8% and 60% separately. Conclusions: Kisspeptin plays important roles in the process of puberty initiation, and also can be a supplementary diagnostic value in the differential diagnosis of puberty initiation.

关键字 The initiation of puberty, Auxiliary diagnosis, Kisspeptin.

分类：9. Endocrinology 内分泌遗传代谢
1433

Novel NPR2 gene mutations identified in patients with short stature repress chondrocyte differentiation by inducing ER stress and the unfolded protein response

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Aims
Natriuretic Peptide Receptor 2 (NPR2) plays a key role in cartilage and bone morphogenesis. NPR2 gene genetic alterations result in three different types of skeletal dysplasia, including acromesomelic dysplasia, Maroteaux type (AMDM), short stature with nonspecific skeletal abnormalities (SNSK) and epiphyseal chondrodysplasia, Miura type (ECDM). We aim to the explore the potential pathogenesis of NPR2 gene mutation causing skeletal dysplasia.
Methods
In our study, five independent Chinese families with familial short stature were recruited. The genetic etiology was identified by whole exome sequencing (WES) and confirmed via Sanger sequencing. Seven NPR2 gene variants were overexpressed in HEK293T and ATDC5 cells to analyze the function, expression and subcellular abnormal localization of mutant NPR2 protein, and the differentiation and apoptosis of chondrocytes.
Results
We identified one de novo (R557C) and six novel variants (G602W; V970F; R767*; R363*; F857S; Y306S). Three patients with heterozygous mutations (G602W; V970F; R767*) were diagnosed with SNSK (height SD score ranged from -2.25 to -5.60), while another two with compound heterozygous mutations (R363* & F857S; R557C& Y306S) were diagnosed with AMDM (height SD score ranged from -3.10 to -5.35). ATDC5 cells with mutant NPR2 gene showed decreased differentiation, as evidence by lower expression of ColII, ColX, and BMP4, and higher expression of Sox9. Moreover, apoptosis rate was elevated in ATDC5 cells expressing mutant NPR2 gene, as indicated by upregulated AnnexinV and cleaved-caspase-3. Functional analysis showed that NPR2 with different mutations except R557C were poorly influenced by N-glycosylation modification plasma membrane localization and ER stress resulting from the accumulation of mutant protein in ER, as shown by higher expression of GRP78 and p-IRE1α.
Conclusion
Taken together, our results provide a novel insight of NPR2 loss of function which could induce chondrocyte apoptosis and repress cell differentiation through ER stress and the unfolded protein response.

关键字 1.short stature 2.NPR2 3.N-glycosylation 4.ER stress

Category: 9. Endocrinology 内分泌遗传代谢
1732456

A Late-onset glutaric acidemia type II patient characterized by muscle weakness and hepatic failure with literature analyzed

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Abstract Content Objective: To investigate the characteristics of the diagnosis and treatment in patients with Late-onset glutaric acidemia type II. **Methods:** To retrospectively analyze the clinical material of a patient with late-onset glutaric acidemia type II admitted to PICU of our hospital and review the associated literature. **Results:** The patient is a 13-year-and-8-month-old female with the clinical manifestations of aggravated progressive proximal muscle weakness, accompanied by vomiting, abdominal pain and liver enlargement. A marked increase of transaminase, bilirubin and creatine kinase was detected and accompanied by hyperammonemia, hypoglycemia and metabolic acidosis. Tandem mass spectrometry(MS/MS) showed increases in various types of acylcarnitines. The muscle biopsy study showed markedly lipid storage myopathy (LSM), and genetic test showed the homozygous mutation in the ETFDH gene. After treatment with Vitamin B2, carnitine, coenzyme Q10 and plasma exchange, the motivate ability and biochemical parameters of the patient returned to normal. **Conclusion:** For patients with aggravated progressive proximal muscle weakness, accompanied by hepatic dysfunction and increased serum creatine kinase, late-onset glutaric acidemia type II should be considered. Raising awareness is decisive in the early diagnosis and treatment of the disease.

Key words Glutaric acidemia type II; Muscle weakness; Hepatic failure; Lipid storage myopathy; ETFDH

Reference

Sleep

睡眠

分类：25. Sleep 睡眠
117

Evaluation of sleep slow wave activity in children's neurocognitive development

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Childhood is an important period of attention, memory, intelligence and other neurocognitive development in life. Normal neurocognitive development can have a positive impact on children's long-term learning and life. Therefore, it is very important to pay attention to the development process of neurocognition in children. However, it is still difficult to evaluate neurocognitive development objectively in children without accurate and efficient index. Sleep slow wave activity, as a kind of EEG measurement index, is of great significance to the evaluation of brain structure and function in children, and it is also a high-quality index to evaluate children's neurocognitive development. This paper mainly reviewed the evaluation of sleep slow wave activity in children's neurocognitive development, aiming to provide reference for exploring the normal and abnormal process of children's neurocognitive development.

关键字 Sleep;Slow wave activity;Children;Neurocognitive development

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Analysis of the characteristics of sleep-disordered breathing in children with neuromuscular diseases

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Abstract: Objective To analyze the characteristics of sleep-disordered breathing(SDB) in children with neuromuscular disease (NMD), so as to improve the awareness of diagnosis and treatment of NMD with SDB. Methods A retrospective analysis was performed for the 18 children with NMD who had finished polysomnography (PSG). Related data was collected for analysis, including demographic characteristics, daily and nocturnal symptoms of SDB, incidence of OSA, pulmonary function and End-tidal carbon dioxide partial pressure (PetCO2). Important sleep parameters and respiratory event were compared with those of non-NMD group(control group). Results In NMD group,16 cases (89%) had SDB-related daily and nocturnal clinical symptoms,and the youngest age of symptoms was 1 year old. The total sleep time and sleep efficiency in the NMD group were significantly lower than those in the control group ($P < 0.05$), the proportion of REM sleep to total sleep time was decreased significantly ($P < 0.05$), the obstructive apnea hypopnea events in the NMD group were increased significantly($P < 0\ 05$). The oxygen decrease occurred in the REM stage ($P < 0\ 05$), the average oxygen saturation in the REM stage was significantly lower than the control group ($P < 0\ 05$). In our study, 17 cases (94%) of NMD with SDB were diagnosed as OSA and the lung function and PetCO2 of all the cases were normal. Conclusion The proportion of SDB in children with NMD is high, SDB can be found in the early stage of NMD, which results in damages of sleeping structure, declining sleep efficiency, and the main respiratory events are obstructive type. Most of the hypoxia events will occur during REM stage.

关键字 Neuromuscular disease; Sleep-disordered breathing; Polysomnography; Child

分类：25. Sleep 睡眠
375

Altered Spontaneous Brain Activity Related to Neurologic and Sleep Dysfunction in Children with Obstructive Sleep Apnea Syndrome

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Childhood Obstructive sleep apnea (OSA) is a common chronic sleep-related breathing disorder in children, which leads to growth retardation, neurocognitive impairments and serious complications. Considering the previous studies about brain structural abnormalities in OSA, in the present study we aimed to explore the altered spontaneous brain activity among OSA patients, using amplitude of low-frequency fluctuation (ALFF), fractional ALFF (fALFF) and regional homogeneity (ReHo) methods based on resting-state functional magnetic resonance imaging (MRI).Thirty-one untreated OSA children and 33 age-and gender-matched healthy children (HC) were included in this study. Compared with controls, OSA group showed significant lower ALFF in the right lingual gyrus, decreased fALFF in the left middle frontal gyrus and increased fALFF in the left precuneus. Decreased ReHo were found in the left inferior frontal gyrus (orbital part) and left middle frontal gyrus. Notably, the mean fALFF value was not only significantly related to the sleep parameters, but also demonstrated the best performance in ROC curve analysis. These findings reveal OSA children associated with dysfunctions in the default mode network, the frontal lobe, and the lingual gyrus, which may implicate the underlying pathologic mechanisms of cognitive impairment. The correlation between the altered spontaneous neuronal activity and the clinical index in patients with OSA provides an early imaging biomarker for the cognitive dysfunction of OSA children.

关键字 obstructive sleep apnea，children，amplitude of low-frequency fluctuation fractional ALFF,regional homogeneity,functional magnetic resonance imaging

分类：25. Sleep 睡眠
394

Characteristics of attentional network in children with sleep disordered breathing

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Objective To investigate the characteristics of attention network and its relationship with sleep in children with sleep disordered breathing (SDB). Methods This was an observational study. Data for the healthy control group were obtained from age- and gender-matched normal children reported in literature. Children with habitual snoring admitted to the Sleep Center, Beijing Children’s Hospital were recruited to SDB group in this study between May 2020 to December 2020. All children aged 6-10 years old and of them 45 were boys and 18 were girls. All subjects underwent an overnight polysomnography (PSG), as well as Attention Deficit Hyperactivity Disorder (ADHD) Diagnostic Scale and an attentional network test adapted to children (child-ANT). All subjects were grouped into primary snoring (20 cases), mild (22 cases) and moderate-to-severe OSA (21 cases) group according to the obstructive sleep apnea hypopnea index (OAHI). Results In total, 63 children were included in the analysis. There were no significant differences in age, gender or body mass index among PS, mild and moderate-to-severe OSA group (all P >0.05). The score of hyperactivity, impulsivity symptom in moderate-to-severe OSA group was significantly higher than that of PS (P<0.05) and mild OSA group (P<0.01). The efficiency of alerting network was higher and the efficiency of orienting network was lower of the mild OSA group than those of the healthy control group (P=0.011, 0.032). Compared with the healthy control group, moderate-to-severe OSA group had lower efficiency of executive control network (P=0.017). Conclusions The function of attentional network was impaired in children with sleep-disordered breathing. Children with mild OSA mainly showed excessive activation of alerting network and reduced efficiency of orienting network. Children with moderate-to-severe OSA mainly showed decreased efficiency of executive control network.

关键字 child，OSA，attention

分类：25. Sleep 睡眠
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Efficiency of two screening tools in diagnosing pediatric Obstructive Sleep Apnea: A prospective cross-sectional study

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Abstract: Objective To evaluate the Efficiency of Pediatric Sleep Questionnaires (PSQ) and Pediatric obstructive sleep apnea Screening Tool (PosaST) in diagnosing pediatric Obstructive Sleep Apnea Syndrome and compare the correlation.
Study Design A prospective cross-sectional study
Methods A total of 75 patients suspected OSA underwent overnight polysomnography (PSG) in West China Second University Hospital, Sichuan University from August 2020 to July 2021 were enrolled and the clinical data were analyzed, including PSG results, PSQ scores, PosaST scores and the basic characteristics data of patients. Based on the apnea-hypopnea index (AHI) from PSG results, the patients were divided into OSA group (n=33) and non-OSA group (n=42). The sensitivity and specificity of each questionnaire was statistically analyzed, receiver operating characteristic (ROC) curve was drawn, and the efficiency of two questionnaires in diagnosing pediatric OSA were compared.
Results 1. There were no significant differences between the basic characteristics of the two groups ($p>0.05$) (Tab.1).
2. There were statistically significant differences in PSG monitoring indicators AHI, OAHI (Obstructive Apnea Hypopnea Index), OAI (Apnea Hypopnea Index), apnea mode, microarousal index and minimum oxygen saturation between the two groups ($p<0.001$), while there were no significant differences in total sleep time, leg movement index and REM sleep times between the two groups ($p>0.05$).
3. The internal consistency test showed the Cronbach's

关键字 Pediatric Sleep Questionnaires, Pediatric obstructive sleep apnea Screening Tool , pediatric Obstructive Sleep Apnea Syndrome

分类：25. Sleep 睡眠
1113

Analysis of Characteristics of Attention Deficit and Hyperactivity-Impulsiveness in Children with Sleep-Disordered Breathing

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Objective To investigate the characteristics of attention deficit and hyperactivity-impulsiveness in children with sleep-disordered breathing (SDB). **Methods** Children aged 4-10 years with snoring or mouth breathing, who admitted to the Sleep Center of Beijing Children's Hospital affiliated to Capital Medical University from May 2020 to June 2021 were selected as the subjects. All subjects completed polysomnography and attention deficit hyperactivity disorder diagnostic scales. According to obstructive sleep apnea hypopnea index (OAHI), children were divided into primary snoring group (OAHI≤1 events /h), mild OSA group (1<OAHI≤5 events /h) and moderate to severe OSA group (OAHI＞5 events /h). The differences of sleep architecture, sleep breathing parameters, attention deficit, hyperactivity-impulsivity and positive incidence of ADHD diagnostic scale were compared in children with different severity SDB. **Results** A total of 239 children with SDB were included, including 76 primary snoring [47 males (61.8%)], 86 mild obstructive sleep apnea (OSA) [55 males (64.0%)] and 77 moderate and severe OSA group [49 males (63.6%)]. The M (Q1,Q3) of ages of children in the three groups were 6.8 (5.7,8.1), 6.6 (5.4,8.4) and 6.6 (5.7,8.3) years old, respectively. There was no significant difference in age and sex among the three groups (all P value 0.05). The body mass index, percentage of non-rapid eye movement sleep to total sleep time and percentage of rapid eye movement sleep to total sleep time, OAHI, arousal index, oxygen desaturation index, average blood oxygen saturation (SpO2) and the SpO2 nadir were statistically different among the three groups (all P value 0.05). Comparisons of the prevalence of attention deficit and positive incidence of ADHD diagnostic scale showed statistically differences among the three groups (all P value 0.05). Subgroup analysis showed that the incidence of attention deficit and hyperactivity- impulsivity in boys was higher than that in girls (P value 0.05). Compared with preschoolers, school-age children have higher prevalence of attention deficit (P value 0.05), whereas there was no significant difference in the incidence of hyperactivity- impulsivity between these two groups (P value 0.05). **Conclusion** The prevalence of attention deficit and hyperactivity-impulsivity in children with sleep disordered breathing is higher than that in the general population, among which both the incidence of attention deficit and hyperactivity-impulsiveness in boys were higher than that in girls, and the incidence of attention deficit in school-age children is higher than that in preschoolers, which should be paid attention to in clinical work.

关键字 children, sleep-disorder breathing, attention deficit, hyperactivity

分类：25. Sleep 睡眠
1136

Decreased RET and PHOX2B expression in iPSC-Derived Neurons in a child with sleep-related hypoventilation

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Our case is a 3years and 2-month-old boy, who had an influenza A virus pneumonia and right upper atelectasis 4 months before. After recovering from the pneumonia, his echocardiography showed the diameter of right atrium increased slightly. On examination, his vital signs were normal. On the night of admission, he showed perioral cyanosis during sleep. His polysomnography, simultaneous transcutaneous oxygen saturation (SpO2) and transcutaneous partial pressure of carbon dioxide (TCPCO2) monitoring showed SpO2 decreased to 82%-85%, TCPCO2 increased to 117.8mmHg during sleep. However, these symptoms go back to normal when he was awake.
The boy was clinical diagnosed as sleep hypoventilation based on these findings. Later, he was treated with non-invasive ventilation all night, and the SpO2 increased to 98%, TCPCO2 decreased to 70mmHg during sleep.
The boy was suspected as congenital central hypoventilation syndrome (CCHS) for an idiopathic failure of the automatic control of breathing, especially during sleep. Then we detected the boy and his parents' the paired-like homeobox gene 2B (PHOX2B) which was the disease-defining gene of CCHS. However, there is no mutation of PHOX2B but receptor tyrosine kinase proto-oncogene (RET) intron14 (c.2608-125C>T) in the boy. We differentiated the neurons of the boy (as a research group) and his mother (as a control group) who had no mutation of RET and PHOX2B gene. There is no significant difference in neuron morphology, length and discharge ability compared with the control group. However, it shows impaired expression of mRNA and protein of RET and PHOX2B. We hypothesize that RET might has a relationship with PHOX2B which could induce sleep related hypoventilation.

关键字 Sleep-related hypoventilation; IPSC; PHOX2B; RET

Category: 25. Sleep 睡眠
1291

Association of Screen Time with Sleep Problems among Preschool Children in Metro Manila

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Abstract Content Filipino children, as young as preschoolers, are becoming increasingly engaged in using electronic media. However, a dearth of local studies on the effects of Screen Time (ST) on preschoolers' health still exists. A review of foreign literature suggests that there is an association between excessive ST and sleep deprivation among preschoolers. To help address this gap in knowledge in the local scene, the present study sought to determine the association between ST and sleep problems among preschoolers in Metro Manila. Specific objectives were: (1) to determine the percent distribution of preschool children according to socio-demographics, media consumption, and prevalence of sleep problems; (2) to evaluate preschoolers' ST according to daytime, nighttime, and total daily duration; (3) to determine the mean sleep duration among those with ideal total ST and those with increased total ST; and (4) to determine the association of increased total ST and sleep problems.

Methods This analytic cross-sectional study involved primary caregivers of preschool children aged 3-5 years in Metro Manila recruited through convenience and chain referral sampling. A total of 399 respondents met the inclusion and exclusion criteria. Online data collection was administered through Google Forms containing the Informed Consent Form, Questionnaire for Primary Caregivers, and Children's Sleep Habits Questionnaire (CSHQ). The Questionnaire for Primary Caregivers was a five-part, 22-item questionnaire adapted from a local study by Gentallan *et al.* in 2019, consisting of the respondents' demographic information, media consumption, sleeping environment, and lifestyle profile. The CSHQ is a 33-item psychological questionnaire with eight subscales (sleep duration, daytime sleepiness, sleep onset delay, bedtime resistance, sleep anxiety, night waking, parasomnias, and sleep disordered breathing) to assess the frequency of behaviors associated with common sleep difficulties of children aged 4-12. Questionnaires were validated by the original authors and a pediatrician. Pilot testing showed that the CSHQ had acceptable full-scale coefficient of 0.718 and subscale coefficient range of 0.157-0.641. Frequency counts and percentages of the sociodemographic data and prevalence of sleep problems were processed via IBM SPSS. Criteria for total sleep disturbance and sleep subscales were used to screen sleep problems. Mean ST, crude odds ratios (OR), confounders and other sleep factors were calculated and controlled via simple and multiple logistic regression, respectively. This study was reviewed and approved by the St. Luke's Medical Center Institutional Ethics Review Committee.

Results Among the 399 respondents, the majority of children were males (53.9%), aged 3-4 years (71.4%) and attended preschool/daycare (54.2%). Results showed an average total ST per day of 4.5±2.6 hours with 2.7±1.6 hours during daytime and 1.8±1.4 hours at nighttime. Majority (94.88%) of participants exceeded the recommended ST (1 hr/day) by the American Academy of Pediatrics.

Majority (88.97%, CI 95% 0.097-0.463) screened positive for total sleep disturbance wherein night wakings (26.82%), sleep disordered breathing (16.04%) and sleep onset delay (15.79%) were the most prevalent. No significant difference was found between

the total sleep duration of preschoolers with ideal and increased ST (ST>1hr/day) (OR 1.018, CI 95% 0.238-4.347; p= 0.981). No significant association was found between increased total ST and total sleep disturbance. When ST duration was analyzed with each of the 8 subscales, only sleep anxiety was significantly associated with increased total ST (OR 0.063, CI 95% 0.004-0.982) where the odds of sleep anxiety were decreased by a factor of 0.063 in those with increased total ST.
Nighttime gadget use (OR 3.182, CI 95% 1.172-8.641) was found to have a 3.182 increase in the odds of experiencing total sleep disturbance.
Conclusion The findings on the average total ST per day of preschool children in Metro Manila was 4.5 hours (2.7hrs for daytime; 1.8hrs for nighttime), exceeding the recommended 1-hour ST for children. Only 5% had ideal ST with TVs and mobile phones as the most frequently used gadgets for media. There appears to be no association between increased ST (ST>1hr) and the overall total sleep disturbance. There were also no associations found between increased ST and sleep problems except for sleep anxiety. Nighttime gadget use in this age group was found to be associated with total sleep disturbance. Confounding factors such as sleeping with lights on, presence of noise during sleep, exercising/playing regularly, eating regular meals/snacks, the child having their own room, and doing homeworks at night were found to be significant predictors of some specific sleep problems and may be subject of further investigation.

Key words Preschool Children, Screen Time, Media Consumption, Sleep problems, Factors in Sleep
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Category: 25. Sleep 睡眠
1349

Natural history and blood pressure outcomes associated with stage-dependent OSA in children: a longitudinal follow-up study

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Abstract Content Most respiratory events in childhood obstructive sleep apnea (OSA) take place during rapid-eye-movement (REM) sleep. This study aimed to describe the characteristics and natural history of childhood REM-OSA and to evaluate the associations between OSA subtypes and blood pressure (BP) outcomes.

Methods This was a prospective 10-year follow-up study of a cohort established for a childhood OSA epidemiologic study. All subjects from the original cohort were invited to undergo polysomnography (PSG) and 24-hour ambulatory blood pressure (ABP) monitoring. REM-OSA was defined with a ratio of obstructive apnea hypopnea index (OAHI) during REM sleep (OAHIREM) to OAHI during non-REM sleep (OAHINREM) ≥ 2. Natural history was observed and linear mixed models were used to assess the associations between OSA subtypes and BP outcomes.

Results 610 participants from baseline were included to study the epidemiology of REM-OSA in childhood. Among children with OSA, 65% had REM-OSA. At 10-year follow-up, 234 were included in the analysis. REM-OSA was more common at both baseline (58/92, 63%) and 10-year follow-up (34/58, 59%). For those with REM-OSA at baseline and persistent OSA at follow-up, majority (72%) remained to have REM-OSA. Compared to those without OSA, subjects with REM-OSA had significantly higher nocturnal SBP (mean difference 2.19 mmHg, 95% confidence interval (CI): 0.12, 4.26; p=0.039) and DBP (mean difference 1.58 mmHg, 95% confidence interval (CI): 0.11, 3.04; p=0.035), and less nocturnal SBP dipping (mean difference -1.84%, 95% CI: -3.25, -0.43; p=0.011), after adjusting for potential confounders. This significant association between REM-OSA and nocturnal SBP dipping was observed at baseline visit only.
Conclusion REM-OSA was found to be a stable phenotype through childhood to young adulthood, and REM-OSA was associated with higher nocturnal BP and a lesser degree of nocturnal SBP dipping in children

Key words Obstructive sleep apnea, children, epidemiology, stage-dependent OSA, rapid eye movement, phenotype, blood pressure
Reference NA

Category: 25. Sleep 睡眠
1388

Parental work arrangements and its impact on children's sleep: Lessons from the SARS-CoV2 pandemic

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Abstract Content Background: Sleep is known to be influenced by several social and cultural factors that represent a complete family environment. The current coronavirus disease (COVID-19) pandemic caused by Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has significantly impacted these factors. The tightened movement restrictions and lockdowns implemented to reduce social interactions in order to curb the spread of virus, have significantly impacted the family environment where parents had to work from home and children had to take their classes online without physically going to school. It remains unknown how these changes, specifically parental work arrangement, influenced the sleep in children. We aimed to evaluate the effects of parental sleep and work arrangements on children's sleep duration during the national lockdown period, referred to as 'Circuit Breaker' (CB), due to COVID-19.

Methods Methods: This was a cross-sectional study carried our between 18 April 2020 to 23 May 2020. It was an anonymous, online questionnaire survey in which eligible parents responded to a survey questionnaire posted on form.sg platform. The eligibility criteria were that of parents aged 21 years and above, with children aged between 3 to 16 years attending preschool, primary or secondary school and residing in Singapore. An additional group of parents with infants and non-school-going children aged between 6 months and 3 years were also invited to participate in the study. Child and parental sleep duration in relation to change in parental work arrangements as reported by parents were evaluated. Descriptive statistics and tests of comparison were used to evaluate data.
Results Results: A total of 593 responses were analyzed from parents of school-going children, and an additional subset of 74 responses from parents with infants and non-school-going children. School-going children (n = 593) had a mean age of 8.68 (SD = 3.65; median 7 years). Both fathers and mothers had gains in sleep (based on self-reported sleep data) during CB, compared to pre-CB. Change in both maternal and paternal sleep duration positively correlated with change in child sleep duration (based on parent-reported sleep data) among all children ($r2 = 0.27$, $p < 0.001$ and $r2 = 0.17$, $p < 0.001$ respectively); pre-schoolers mirrored their mothers' sleep more closely. Parents who changed to working from home during the CB (compared to working from outside home previously) had the greatest gains in sleep during this period.
Conclusion Conclusions: Greater gains in sleep in parents was associated with working from home during CB. Child sleep duration mirrored gains in parental sleep, especially in pre-school and primary-school-going children. Optimising parental sleep may therefore be one of the means to improve child sleep.

Key words Child, Sleep, Parental Work, Parental Sleep
Reference nil

Category: 25. Sleep 睡眠
1390

Academic start times and its impact on children’s sleep duration: Lessons from school closure during the SARS-CoV2 pandemic

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Abstract Content Background: The COVID-19 pandemic that emerged in the month of January 2020, led to the lockdown of cities and countries and significant changes in daily activities of people of all ages. School-going children had to resort to home based learning when schools were closed from 7th April to 1st June 2021. This was associated with unprecedented changes in their routines; including changes in sleep-wake times as a result of removal of school commutes and later school start times, both of which are known to impact sleep duration in children. We aimed to study the sleep habits of school-going children before and during school closure in the national lockdown period (called ‘Circuit Breaker’ or CB in Singapore) due to the COVID-19 pandemic, to evaluate the impact of school routines on sleep in our children.

Methods Methods: A cross-sectional study was carried out from 18 Apr -19 May 2020. An anonymous, online, population-based survey questionnaire where parents aged 21 years and above who had children aged between 3 and 16 years attending pre-school, primary or secondary school (equivalent to kindergarten, middle and-high school) and residing in Singapore were invited to participate via social media invitations. The questionnaire included questions related to sleep duration and various other daily activities such as academic activities, physical exercise, and screen time pre-CB and during CB.

Results Results: A total of 593 responses were received. Pre-CB, the overall mean (SD) sleep duration of the study population was 9.01 (1.18) hours on weekdays and 9.99 (0.94) hours on weekends. During CB, mean (SD) sleep duration overall was 9.63 (1.18) hours. Although children generally went to bed later (mean 0.65 h later), they woke up even later during CB (mean 1.27 h later), resulting in a longer sleep duration (mean increase of 0.35 h). This was most evident in secondary school children (mean increase of 0.70 h). Children attending private schools (which had later start times) had increased sleep duration (mean 10.01 (SD 0.89) hours pre-CB and 10.05 (SD 0.93) hours during CB) compared to public schools (mean 9.05 (SD 0.91) pre-CB and 9.49 (SD 1.22) hours during CB).

Conclusion Conclusions: School closure from the COVID-19 pandemic resulted in longer sleep duration in school-going children. Later school/academic activity start times can significantly impact on children's sleep duration.

Key words Child Sleep, School start times, School closure, Covid-19
Reference Nil

Category: 25. Sleep 睡眠
1440

Photogrammetry As A Screening Tool For Childhood Obstructive Sleep Apnoea - A Pilot Study

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Abstract Content Cranio-facial profile is an important component in the aetiology of childhood obstructive sleep apnoea (OSA). Different craniofacial features can be captured by photogrammetry, which is making measurements by photographs. Whether photogrammetry findings together with clinical parameters would yield a clinically acceptable screening tool for childhood OSA has not been explored. Therefore, this study aimed to develop a prediction model for childhood OSA using both clinical parameters and photogrammetric craniofacial features.

Methods Prepubertal children suspected of OSA were recruited. All subjects underwent craniofacial photogrammetry and overnight polysomnography. Data was split into 70% training data and 30% test data. The prediction models were built from the training data using logistic regression and evaluated on the test data using receiver operating characteristic curve analysis.

Results This study included 90 children (mean age: 8.2 ± 1.6 years, 66 males). Non-OSA, mild OSA and Moderate-to-severe (MS) OSA groups consisted of 32, 31, and 27 subjects, respectively. Four prediction models were built. Model 0 was built with only clinical measurements which included age, sex, BMI z-score and the presence of large tonsils as predictors (AUC = 0.683). Models 1 and 2 used clinical measurements and one photogrammetric feature, which was the maxillary-mandibular relation angle (sn-n-sl) for model 1 (AUC = 0.778), and the anterior mandibular height to whole face length ratio (sto-gn/n-gn) for model 2 (AUC = 0.806). Model 3 used clinical measurements and the two photogrammetric features, giving the highest accuracy (AUC = 0.861).

Conclusion Craniofacial features obtained from photogrammetry could improve the prediction accuracy for childhood OSA.

Key words OSA, photogrammetry

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Category: 25. Sleep 睡眠
1490

Obstructive Sleep Apnea in Children with Thalassemia

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Abstract Content Obstructive sleep apnea (OSA) are the major problems associated with sleep quality and quality of life in children. Thalassemia is a common genetic disease with facial bone deformities which may lead to OSA. This study aimed to investigate the prevalence and associated factors of obstructive sleep apnea in paediatric patients with thalassemia.

Methods A cross-sectional study was conducted in 113 thalassemia patients, aged under 15 years old, who visit Chonburi hospital during September 2019 and November 2019. Thai version quality of life questionnaire for OSA (OSA-18) was used for OSA screening. Overnight polysomnography (PSG) was further conducted in patients with suspected OSA. Data were analyzed in descriptive statistics (percentage, mean and standard deviation) and correlations (Chi-square and Fisher's exact test).

Results Of 113 thalassemia patients, the prevalence of OSA from OSA-18 questionaire was 9.73%. 11 patients were undergone PSG. 7 had mild OSA and 4 had moderate OSA with mean AHI of 2.1 per hour and 6.4 per hour respectively. Significant statistical factors associated with OSA were co-existing allergic rhinitis (p-value=0.012) and high serum ferritin level (p-value=0.020).

Conclusion Thalassemia patients were at risk of developing OSA. Screening of OSA symptoms and PSG would be recommended.

Key words Thalassemia, obstructive sleep apnea, polysomnography

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分类：25. Sleep 睡眠
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Emotion Recognition in children with OSA

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Background
Impaired emotional processing, including reduced emotion facial expression and defective emotion recognition, has been reported in adult Obstructive Sleep Apnea (OSA). There are many relevant studies done on adult populations, but fewer done on children. Childhood is a crucial period of social development, and emotion recognition is an important first step in social communication. Facial emotion recognition paradigm was employed in this study to whether there is a general emotion recognition impairment in children with OSA.
Method
18 children with OSA and 18 healthy controls completed an emotion recognition task and 1night of polysomnographic evaluation. Accuracy rates and reaction times were recorded and analyzed using repeated-measures analysis of variance.ResultsThere was a main effect of group on accuracy [$F(1, 18) = 4.98$, $p = 0.037$, $\eta p^2 = 0.20$] and RT [$F(1, 18) = 15.86$, $p = 0.001$, $\eta p^2 = 0.44$] , which indicated that accuracy was higher and RT was faster in the control group. There was a main effect of emotion on RT [$F(1, 18) = 10.61$, $p = 0.004$, $\eta p^2 = 0.35$], which indicated that RT to happy faces was faster than to sad faces. There was no interaction between group and emotion.ConclusionsChildren with OSA have impairments in facial emotion recognition. This impairment is may indicate that emotion recognition may lead to social and emotional problems in these children.

关键字 Emotion recognition; Children; OSA; Social cognition

分类：25. Sleep 睡眠
1656

Efficacy analysis of drug intervention in children with mild to moderate obstructive sleep apnea hypopnea syndrome

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Objective: Children with obstructive sleep apnea hypopnea syndrom (OSAHS) refers to ventilatory disorders caused by partial or complete obstruction of the upper airway, which disrupts children's normal ventilation and sleep structure, leading to endocrine and metabolic disorders, neurological recognition Knowing injuries, abnormal maxillofacial development, and long-term increased risk of cardiovascular accidents, the early detection, early diagnosis and early treatment of OSAHS in children are of great significance to reduce complications and improve prognosis. In order to investigate the efficacy of mometasone furoate nasal spray and montelukast sodium chewable tablets in children with mild to moderate OSAHS, and to find a safe and effective treatment plan for children with OSAHS, this paper describes the comparison result differ in the treatment between the combined drug group and the single drug group during the same period. Methods: This study retrospectively analyzed the symptoms of waking up at night, mouth breathing, snoring and other symptoms at the Pediatric Center of the First Affiliated Hospital of Xinjiang Medical University from December 1th, 2018 to October 31th, 2020, and improved sleep monitoring to confirm the diagnosis as mild to moderate. Children with mild to moderate OSAHS were randomly divided into nasal mometasone furoate nasal spray group (nasonide group) 48 cases, montelukast sodium group (singulirine group) 54 cases, combined There were 58 cases in the medication group, and general data of the children were collected: gender, age, weight, and BMI. All children recorded the results of sleep monitoring before and after 3 months of treatment and the disease specific quality of life for children with obstructive sleep apnea 18 items survey (OSA-18) scores. Results: ①After drug treatment, the AHI of the combined drug group was lower than that of the pre-treatment and the same period of the single drug group, and the LSaO2 of the combined drug group was higher than the pre-treatment and the same period of the single drug group (P<0.05), while the AHI, LSaO2 nasonide group compared with singulirine group, the difference was not statistically significant (P>0.05); ②After drug intervention, above three groups were lower in sleep disorders, emotional conditions, physical symptoms, impact on guardians, daytime functional status, and total scores. Before treatment, and the scores of the combination group were lower than those of the single ones (P<0.05).There was no statistically significant difference in poor scores of Neshuna group in poor mood, daytime functional status and singulirine group in mood(P>0.05); ③The effective rates of treatment among the three groups were 47.92%, 60.42%, and 89.58%, respectively. There were differences between the combination medication group and the Nesunar group and the Shunerning group (P<0.05), but there is no statistical difference between the Nesuna group and the Shunerning group (P>0.05). Conclusion: Both single and combined drugs can effectively reduce AHI and increase LSaO2. The efficacy of combined drugs is better than single drugs; single and combined drugs can significantly improve the quality of life, and the combined drug group is better than the single drug group.

关键字 Obstructive sleep apnea hypopnea syndrome, OSAHS, Children, Nasal corticosteroids, Montelukast sodium

分类：25. Sleep 睡眠
1679

Maternal sleep during late pregnancy, offspring DNA methylation and adiposity status at 2 years old: a prospective cohort study

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Aim: To explore the effect of maternal sleep during late pregnancy on offspring’s adiposity at 2 years of old, and the potential mediation effect of cord blood DNA methylation.
Method: A total of 2962 healthy and singleton pregnancy women from Shanghai birth cohort (SBC) and Shanghai Sleep Birth Cohort Study (SSBC) were included in the study. Maternal night sleep duration (NSD), quality and midpoint were estimated by questionnaire in late pregnancy and offspring’s weight, length and skinfold thickness were measured at 2 years old. In the 171 subsample participants from SSBC, genome-wide DNA methylation were measured in cord blood. Multivariable linear regression was used to evaluate the associations between maternal sleep and offspring adiposity and the role of DNA methylation in the association between maternal sleep and offspring adiposity was explored by mediation analysis.
Result: The NSD in our study was about 9.24±1.13h and the midpoint was 3.03±0.83. About 25.72% pregnant women were reported have experienced poor sleep quality during pregnancy. After adjusted for covariates, later sleep midpoint of mother during late pregnancy was associated with increased skinfold thickness of offspring (β=0.61, 95%CI: 0.34-0.87, $p<0.001$) at 2 years old. There were 45 differential methylated probes (DMPs) associated with maternal sleep midpoint, and one of which mediated the effect of maternal sleep midpoint and skinfold thickness of offspring at 2 years old. However, in our study, we didn’t find the effect of maternal NSD and self-reported sleep quality on offspring adiposity and cord blood DNA methylation.
Conclusion: Later sleep midpoint during late pregnancy would increase skinfold thickness of offspring at 2 years old. And the altered cord blood DNA methylation may mediate the effect of maternal sleep midpoint on offspring adiposity.

关键字 maternal sleep, DNA methylation, adiposity

Clinical Epidemiology

临床流行病

分类：5. Clinical Epidemiology 临床流行病
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Associations between obesity and incident risk of hyperuricemia in children

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【Abstract】 Objective To investigate the relationships between obesity and the incidence risk for hyperuricemia in children. Methods Data were obtained from School- based Cardiovascular and Bone Health Promotion Program. In 2017, a total of 15 391 children aged 6~16 years in Beijing were selected through stratified cluster sampling method at baseline survey. Follow-up investigation was conducted in 2019. Logistic regression model was used to analyze the relationships of obesity and change in obesity status and incidence risk for hyperuricemia. Results A total of 8 178 participants (4 088 boys, 4 090 girls) were involved in the analysis, the average age of children was 10.9±3.3 years at baseline survey. The adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of incidence risk for hyperuricemia in the obese and extremely obese were 4.23(3.62~4.95) and 8.41(6.74~10.49), respectively. With the increase of FMP at baseline, the adjusted OR and 95%CI of incidence for hyperuricemia in the fourth quartiles of the FMP was 5.01(4.19~5.98). The ORs and 95%CIs were 2.49(1.92~3.22), 2.41(1.78~3.27) and 4.94(4.28~5.71) for hyperuricemia in the BMI groups of obesity recover, newly diagnosed obesity and persistent obesity. The ORs and 95%CIs were 2.44(1.96~3.05), 2.22(1.74~2.84) and 4.65(4.02~5.38) for hyperuricemia in the FMP groups of obesity recover, newly diagnosed obesity and persistent obesity. The gender-stratified analysis showed that the similar results. Conclusions Childhood obesity was associated with increased incidence risk for hyperuricemia. Maintaining optimal weight by children might contribute to the early prevention of hyperuricemia.

关键字 Children; Obesity; Hyperuricemia; Cohort study

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Causal evidence of body mass index, fat mass percentage and waist-to-height ratio on cardiometabolic traits among children: A Mendelian randomization study from BCAMS

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Aims/hypothesis observational studies reveal that obesity and obesity relevant measures are associated with cardiometabolic disease. However, these findings may inevitably suffer bias because of residual confounding and reverse causation. Mendelian randomization (MR) employs genetic variants as instrumental variables to address these biases, while it is utilized mainly in adults for causal inference. Therefore, we applied MR to explore and compare the causal relationships of general obesity (measured by BMI), adipose obesity (measured by fat mass percentage (FMP)) and central obesity (measured by waist-to-height ratio (WHtR)) with cardiometabolic traits among children.

Methods We conducted a MR analysis in 3266 unrelated children from Beijing Children and Adolescents Metabolic Syndrome Study (BCAMS). A total of 28 SNPs that identified by previous genome wide association studies was genotyped using TaqMan Allelic Discrimination Assays with the 7900 Sequence Detection System. The genetic risk score of BMI, FMP and WHtR were performed as genetic instruments to explore the causal associations of genetically predicted BMI, FMP and WHtR with cardiometabolic traits, including blood pressure, glycemic traits and blood lipids. The comparisons of causal effects of BMI, FMP and WHtR on various cardiometabolic traits were evaluated by receiver operating characteristic curves (ROC).

Results Each genetically predicted 1-SD increment in BMI, FMP and WHtR were significantly associated with 14.37 mmHg, 11.47 mmHg and 6.99 mmHg increment in systolic blood pressure (SBP), 7.87 mmHg, 7.90 mmHg and 2.23 mmHg increment in diastolic blood pressure (DBP), 0.204 mmol/L, 0.113 mmol/L and 0.188 mmol/L increment in log-transformed fasting plasma glucose (FPG), 0.133, 0.231 and 0.073 increment in log-transformed HOMA-β, and 0.048 mmol/L, 0.051 mmol/L and 0.014 mmol/L decrease in log-transformed high-density lipoprotein cholesterol (HDL), respectively (all $P < 0.05$). The ROC indicated that BMI and FMP showed stronger effects on SBP, DBP, HOMA-β and HDL than WHtR (all $P < 0.05$).

Conclusions/interpretation The genetic predisposition to elevated BMI, or FMP, or WHtR was a causal risk factor for cardiometabolic traits by virtual of MR approach. When compared with central obesity, general obesity and adipose obesity might own stronger effects on blood pressure and blood lipids among children.

关键字 Body mass index; Fat mass percentage; Waist-to-height ratio; Cardiometabolic traits; Mendelian randomization

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Vitamin D trajectories and risks of cardiometabolic abnormalities during childhood and adolescence: a population-based prospective cohort study

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Objective: Vitamin D deficiency has recently evolved as a highly prevalent situation affecting almost every third of children worldwide. The impact of vitamin D on cardiovascular health in children remains unclear and recent studies investigating relations between them obtained inconsistent results. We aimed to analyze the associations of the longitudinal trajectory of vitamin D status with the risks of cardiometabolic abnormalities (including hypertension, hyperglycemia, and dyslipidemia) during childhood.
Methods: Data was obtained from a population-based prospective cohort study. A total of 10482 participants who had 25(OH)D concentrations and cardiometabolic parameters data both in the baseline and follow-up surveys were included in this analysis. The 25(OH)D concentrations, waist to height ratio, blood pressure, blood lipids, fasting blood glucose (FBG), and insulin were determined. We classified four possible trajectories based on vitamin D status in two surveys. Adjusted risk ratios were calculated to assess the relationships between the risk of cardiometabolic abnormalities and vitamin D trajectories.
Results: Overall, 35.1% and 24.2% of participants had vitamin D deficiency at baseline and follow-up survey, respectively, and 15.1% of participants were with a persistent vitamin D deficiency condition. Children who maintained persistent vitamin D deficiency status at baseline and follow-up had highest risk of high TC (RR [95%CI]: 1.61 [1.18, 2.19], Ptrend<0.001), high LDL-C (RR [95%CI]: 1.53 [1.04, 2.27], Ptrend=0.046), and high TG (RR [95%CI]: 1.96 [1.34, 2.87], Ptrend=0.003). Children who shifted from vitamin D non-deficiency at baseline to deficiency at follow-up had a 2.09-fold increased risk (95%CI: 1.36, 3.23) for high TG compared with those who were free of vitamin D deficiency both at baseline and follow-up (reference group). However, children who altered vitamin D status from deficiency to non-deficiency during follow-up still had a higher risk of high TC than the reference group (RR [95%CI]: 1.61 [1.18, 2.19]).
Conclusions: These results suggest that the persistence of vitamin D deficiency may increase the risk of dyslipidemia in children, and vitamin D deficiency possibly had short or long-term effects on different subtypes of dyslipidemia.

关键字 vitamin D; cardiometabolic abnormality; cohort study; children

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Status of red blood cell folate, serum folate, vitamin B-12 and homocysteine in pregnancy-preparing couples of reproductive age: a large cross-sectional study

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Background
Red blood cell (RBC) folate, serum folate, vitamin B-12, and homocysteine (Hcy) levels are commonly accepted biomarkers of folate status. The protective effects of folate on birth defects were well-established, but little is known on biomarker status among the pregnancy-preparing couples.
Objective
This study was to assess the metabolically status of RBC folate, serum folate, vitamin B-12, and Hcy in pregnancy-preparing couples in a folic-acid unfortified population.
Methods
The cross-sectional data were from an ongoing cluster-randomized controlled trial from 2018 to 2021. RBC folate, serum folate, vitamin B-12, and Hcy status were analyzed in pregnancy-preparing couples. The distribution of RBC folate, serum folate, vitamin B-12, and Hcy were skewed and log-transformed. RBC folate level <340nmol/L and serum folate level <10 nmol/L were folate deficiency indicators. RBC folate levels over 906 nmol/L and serum folate over 15.9 nmol/L were associated with the greatest reduction of NTDs, so the cut-offs were defined as folate insufficiency. The threshold for identifying vitamin B-12 deficiency and marginal insufficiency was <148pmol/L and 148-221 pmol/L. Serum Hcy >15 nmol/L was the indicator of Hyperhomocysteinemia. Associations analysis were conducted by genders considering the differences in demographics and lifestyle factors between genders. Linear regression (log-transformed concentrations) was used to examine the associations of those factors with biomarker concentration differences, and the percentage changes in geometric mean concentrations and 95% CIs were reported. Logistic regression models were used to assess the associations of those factors and the risk of RBC folate, serum folate, vitamin B-12 deficiency and insufficiency, and Hyperhomocysteinemia, respectively. Correlations of biomarkers within couples were determined using Spearman correlation.
Results
The geometric mean concentrations of RBC folate, serum folate, vitamin B-12 and Hcy were 490.6(485.0-496.3)nmol/L, 20.1(19.8-20.3)nmol/L, 353.8(350.7-357.0)pmol/L, and 7.5(7.5-7.6) umol/L in women and 405.5(401.3-409.7)nmol/L, 13.5(13.4-13.7)nmol/L, 277.1(274.6-279.5)pmol/L, and 12.0(11.9-12.2)umol/L in men. RBC folate deficiency and insufficiency prevalence were 18.9% and 90.1% in women and 32.2% and 96.6% in men. Serum folate deficiency and insufficiency prevalence were dramatically higher in men than women (26.5% vs. 7.3% and 65.5% vs. 31.4%). The prevalence of vitamin B-12 marginal deficiency and Hyperhomocysteinemia were significantly higher in females. Age and folic acid supplement use were positively associated with RBC and serum folate status, whereas smoking decrease about 10% serum folate concentrations. BMI over 24 kg/m2 decrease 4.9%-14.6% serum folate concentration in women but increase 3.8%-6.7% RBC folate concentration in men. Concentrations of RBC folate, serum folate, vitamin B-12, and Hcy were closely correlated within couples.
Conclusion

Folate status in most pregnancy-preparing couples was insufficient for preventing birth defects, especially in males. Concentrations of RBC folate, serum folate, vitamin B-12, and Hcy are closely correlated within couples. These findings call for attention to the insufficiency of folate status and powerful strategies to improve the folate status of the pregnancy-preparing population, especially for younger people, smokers, and those with abnormal BMI.

关键字 RBC folate, serum folate, Hcy, vitamin B-12, Cross-sectional study

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Investigation on knowledge, attitude and practice of antibacterial drugs in parents of children in Pinggu district, Beijing

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Objective: By investigating the knowledge, attitude and practice of children’s antibacterial drugs among parents in Pinggu District, Beijing, we try to find out the misunderstanding about antibacterial drugs and incorrect antibacterial drugs practice of children’s parents, and to analyze related influencing factors, to provide reference basis for health promotion and education.

Method：From February to March, 2021, a questionnaire survey was conducted among parents of children aged 0-7 in 40 kindergartens and maternal and child health care centers in Pinggu District, Beijing by convenience sampling. With the help of the Questionnaire Star survey software, parents were guided to fill in the electronic questionnaire online under the premise of obtaining the informed consent of children's parents. The results of the questionnaire platform were imported into Excel software, and the final data was analyzed by SSPS software. Mean, median and percentage were used as descriptive statistics, chi-square test was used for univariate analysis, and binary logistic regression model analysis was used for multivariate analysis. P <0.05 was considered statistically significant.

Results:. A total of 4243 children’s parents participated in this study, and finally a total of 3,415 valid questionnaires were collected, with an effective rate of 80.48%.

Only 36.3% of parents knew that antibacterial drugs were ineffective in treating viral infections. About 45.3% of children's parents believe that taking antibacterial drugs can speed up the recovery of upper respiratory tract infections.The antibacterial drugs knowledge median score was 10, with 60% of parents scoring above 10. Logistic regression analysis indicated that the respondents were female (OR= 1.377,95%CI:1.144-1.657, P=0.001), and the higher education level (OR= 5.435, 95%CI:1.849-15.977, P=0.002; OR=7.924,95%CI: 2.724-23.047, P<0.001;OR= 11.289,95%CI:3.879-32.853,P<0.001;OR=16.892, 95% CI: 4.851-58.818, P<0.001), the only child (OR=0.74,95%CI: 0.580 - 0.942 , p=0.015), higher the per capita monthly income of the family (within the range from 3000 yuan to 50000 yuan) (OR=1.268,95%CI:1.002-1.605, P=0.048; OR=1.337, 95%CI: 1.051 -1.701, p= 0.018;OR=1.648,95%CI:1.232-2.204,p=0.001; OR=1.981, 95% CI: 1.188-3.304, P=0.009), parents had higher antibacterial drugs knowledge scores. 81.3% of children's parents store antibacterial drugs at home. In the last 12 months, 15.5% of parents had bought antibacterial drugs without prescription, and 14.3 % of parents had given antibacterial drugs to their children without medical advice. Logistic regression indicated that the gender was female (OR=0.713,95%CI:0.550-0.922, P =0.01), denied the ability to independently decide the type of antibacterial drugs(OR=0.712,95%CI: 0.568 - 0.894,p=0.002), denied having purchased antibacterial drugs without a prescription within 12 months (OR= 0.113, 95%CI:0.090-0.142, P <0.001); denied having stored antibacterial drugs at home (OR=0.217,95%CI: 0.130 to 0.361, P <0.001), denied having dissatisfied with their doctors' refusal of antibacterial drugs requests (OR=0.819, 95%CI: 0.734-0.913, P <0.001) , parents were less likely to self-administer antibacterial drugs to their children. Parents who did not follow the

doctor's instructions when administering antibacterial drugs to their children (OR=1.363,95%CI:1.234-1.507, P <0.001) were more likely to self-administer antibacterial drugs.
Conclusion: In Pinggu District, Beijing, parents' knowledge of antibacterial drugs still needs to be improved, Although the proportion of antibacterial drugs self-medication and buying antibacterial drugs without prescription is relatively low, there are still other improper use of antibacterial drugs, such as storing antimicrobial drugs, increasing or decreasing the dosage by themselves, and stopping drugs in advance.

关键字 Parents; antibacterial drugs; KAP; self-medication; Influencing factors

分类：5. Clinical Epidemiology 临床流行病
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Retrospective Study of an Adenovirus Pneumonia Outbreak in Shenzhen in 2017

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Objective Human adenoviruses (HAdVs) are associated with respiratory, gastrointestinal, ophthalmological, genitourinary, and neurological infections. HAdVs associated with lower respiratory tract infection endanger children's health due to their poor prognosis, high mortality, severe complications, and serious sequelae.To explore the clinical features of adenovirus pneumonia in children and to provide evidence for timely diagnosis and treatment.
Methods We retrospectively reviewed 57 children diagnosed with adenovirus pneumonia between April and July 2017 in Shenzhen Children's Hospital. The epidemic, clinical, laboratory, radiological features, and treatment outcome of these patients were analyzed.
Results The incidence of severe adenovirus pneumonia was found to be higher in patients who were ≤ 2 years old, had higher CRP and PCT levels, had atelectasis shown on chest CT, or developed extrapulmonary complications. The duration of fever and hospital stay of PB patients were shorter than those of non-PB patients (P < 0.05). On chest CT, PB patients mainly presented with segmental atelectasis and pleural effusion, while non-PB patients mainly presented with bilateral diffusive opacity.
Conclusion In summary, during the outbreak of adenovirus pneumonia in Shenzhen, the epidemic seasons were spring and summer, and the dominant type of HAdV in severe pneumonia was HAdV-B7. When chest radiological examination shows atelectasis and pleural effusion, physicians should consider the likelihood of PB. BAL performed promptly could reduce the duration of fever and hospitalization. The bronchoalveolar lavage fluid sample and Metagenomics next-generation sequencing method should be considered to analyze the pathogens when the conventional approach is failed. However, large-scale prospective clinical studies are needed to determine if BAL combined with IV methylprednisolone could reduce the mortality rate and incidence of sequelae in children with severe adenovirus pneumonia.

关键字 children, adenovirus pneumonia, plastic bronchitis

分类：5. Clinical Epidemiology 临床流行病
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The prevalence of mycoplasma pneumoniae in upper respiratory tract infection, bronchitis, herpangina and pneumonia in children and comparison of laboratory test results from a Chinese children’s hospital

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Objective The role of this study was to compare and analysis the prevalence of mycoplasma pneumoniae (Mp) in upper respiratory tract infection (URI), bronchitis, herpangina and pneumonia and the laboratory test results in children.
Methods The mindray BC-7500 automatic peripheral blood routine analyser was applied to analysis leukocytes (WBC), neutrophile granulocyte (NEU), lymphocyte (LYM), monocyte (MON) and C-reactive protein (CRP). Colloidal gold immunochromatography was performed to detect Mp IgM in the serum to reflect the Mp infection.
Results The numbers of cases of URI, bronchitis, herpangina and pneumonia included in the study were 350、350、160 和 100, and the positive rates of Mp infection were 11.34%（40/350）、9.71%（34/350）、8.75%（14/160）和 11.00%（11/100）, respectively. There was no significant difference among the positive rates. P=0.782. The results of WBC, NEU and CRP of Mp positive and negative cases were 9.78±3.80 and 10.79±4.31, 5.89±3.29 and 6.73±4.11, 5.81±7.27 and 8.67±13.46, respectively. The results of WBC, NEU and CRP of Mp positive cases were significantly lower than those of negative cases, with P=0.026、P=0.049 and P=0.038, respectively. The WBC of URI, bronchitis, herpangina and pneumonia with Mp infection were 9.17±3.43, 9.22±3.78, 12.51±3.67 and 10.20±3.54 respectively, and the WBC of herpangina was significantly higher than that of URI (P=0.004) and bronchitis (P=0.006); the NEU results were 5.56±2.79, 5.10±3.26, 8.50±3.08 and 6.19±3.52 respectively, and the NEU of herpangina was significantly higher than that of URI (P=0.003) and bronchitis (P=0.001); the MON results were 0.43±0.71, 0.31±0.11, 0.60±0.27 and 0.37±0.17 respectively, and the MON of URI was significantly higher than bronchitis (P=0.003), and the MON of herpangina was significantly higher than that of URI (P=0.006), bronchitis (P=0.000) and pneumonia (P=0.003); the CRP results were 4.52±6.08, 3.09±3.47, 12.82±9.77 and 10.01±8.32 respectively, and the CRP of herpangina was significantly higher than that of URI (P=0.000) and bronchitis (P=0.000), and the CRP of pneumonia was significantly higher that of bronchitis (P=0.003).
Conclusion There was no difference in the prevalence of Mp in URI, bronchitis, herpangina and pneumonia. The levels of WBC, NEU and CRP were lower in cases with Mp infection; the levels of WBC、NEU、MON and CRP were all higher in herpangina with Mp infection, and higher in bronchitis with Mp infection.

关键字 Mp； children； CRP； blood routine test

分类：5. Clinical Epidemiology 临床流行病
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Changing trajectory of serum uric acid among children and adolescents aged 4-19 years

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Background and aims: According to epidemiological surveys, serum uric acid (SUA) concentration in children is lower than in adults. At present, it is still unclear for the development of SUA from children to adults. This study aims to describe the changing trajectory of SUA in children and adolescents aged 4-19 years.
Method: We pooled 11 population-based studies in China with measurements of SUA on 45,769 participants aged 4 to 19 years. Using generalized additive models for location, scale and shape (GAMLSS), we smoothed the curve of SUA with age, and finally displayed the changing curves of SUA from 4 to 19 years old by sex and weight status.
Results: In overall population, SUA increased rapidly with age and then remained stable. The SUA curve of boys and girls remained consistent before the age of 10. SUA levels reached to plateau at 10 years of age in girls, while continued to increase to peak at 16 years of age in boys, resulting in significant gender differences in SUA levels after the age of 10. With the increase of BMI, the concentration of SUA and the slope of the curves also increased. In non-overweight and overweight boys, SUA peaked at age 16, while in obese boys, the growth rate of SUA slowed down at the age of 14, but the SUA level continued to increase with a low slope. In girls, SUA levels in different weight groups tend to be stable after 10 years old.
Conclusions: The changing trajectory of SUA is significantly different between boys and girls, and increased BMI will change the growth curve of SUA from childhood to adulthood. Understanding the changing trajectory of SUA and its influencing factors is of great significance for the prevention and control of hyperuricemia in children and adolescents.

关键字 Uric acid, Children, Adolescents, Changing trajectory, Obesity

分类：5. Clinical Epidemiology 临床流行病
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Rapid responses of obesity measures, cardiometabolic profiles and gut microbiota to intermittent calorie restriction versus carbohydrate restriction in youths: a randomized trial

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Objective
We aimed to investigate the short-term responses of obesity measures, glucose and lipid metabolism and gut microbiota alterations to intermittent calorie restriction (ICR) and low carbohydrate diet (ILCD) in the younger population.
Methods
This 14-day exploratory randomized trial included 20 participants aged 9-30 with at least one of overweight or obesity, prediabetes, dyslipidemia, or elevated blood pressure. Participants were randomly allocated to the ICR group receiving caloric restriction (500-600 kcal/d) for two consecutive days per week, or the ILCD group receiving carbohydrate intake ≤50g/d for seven non-consecutive days within two weeks. The changes in anthropometrics, glycemic factors, lipid profiles and gut microbiota composition from baseline to day 14 were measured.
Results
Compared to the baseline levels, ICR intervention significantly reduced body weight by 1.22 kg (95%CI: -1.80 to -0.64), fasting insulin by 4.24 mIU/L (-7.85 to -0.62), HOMA-IR by 1.04 (-1.91 to -0.18), area under the curve of 2h-postprandial glucose by 78.56 mmol*min /L (-134.60 to -22.51), and HDL-C by 0.17 mmol/L (-0.29 to -0.06). However, the reductions were not significantly different from those found in the ILCD group. ILCD reduced TG by 0.22 mmol/L (P=0.06), increased LDL-C by 0.47 mmol/L (P=0.006) and TC by 0.30 mmol/L (P=0.17), the changes of LDL-C and TC significantly differ from the ICR. The relative abundance of Actinobacteria (β=-3.88, -6.61 to -1.16) and Bifidobacterium (β=-3.62, -6.24 to -1.00) significantly reduced by ILCD but did not alter to ICR, and the reductions showed significant mediation effect in the fasting glucose responses to ILCD (P=0.03).
Conclusions
Short-term ICR and ILCD induce similar favorable changes in body weight and glucose regulation but different alterations in lipid profile and gut microbiota composition.

关键字 Intermittent calorie restriction; Intermittent calorie restriction; Youths; Randomized trial

分类：5. Clinical Epidemiology 临床流行病
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Clinical characteristics of pediatric hypertension based on the hospital records: A multicenter retrospective study

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Background: Most information describing clinical hypertension (HTN) in children comes from single-center reports, while few multicenter studies have been conducted in China. Therefore, the primary objective of the present study was to better understand the clinical characteristics and causes of pediatric HTN in China.
Methods: Medical records of inpatients with HTN were collected and reviewed from 9 tertiary children's hospitals during 2010 to 2020 in China. Patients with HTN were divided into three groups based on initial diagnosis (primary, secondary, and unclear type of HTN). Possible secondary causes were found from the medical records of patients with unclear type of HTN and reclassified them as primary or secondary HTN. Demographic, anthropometric and etiological information were compared in patients with different types of HTN using t test, Mann–Whitney U test and $\chi 2$ test.
Results: A total of 5,372 inpatients aged 0-18 years were discharged from the 9 centers. Among them, 833 (15.5%) had primary HTN, 899 (16.7%) had secondary HTN, and 3,640 (67.8%) with unclear type of HTN. After identifying secondary causes and reclassifying patients with HTN, the ratio of primary to secondary HTN was 1:1.6 (38.1% vs. 61.9%). Compared with patients had primary HTN, children with secondary HTN were younger (0~5 ages vs. 6~17 ages), more likely to be female (43.2% vs. 23.2%, $P < 0.001$) and had longer lengths of stay (The median duration was 12 days vs. 8 days, $P < 0.001$). However, those with primary HTN had a significantly older age at diagnosis, 62.0% of children with primary HTN had family history of HTN, and 92.7% of them were overweight or obese. In patients with secondary HTN, the most common cause was renal disease (42.7%), followed by rheumatic autoimmune diseases (17.0%) and neurologic diseases (11.9%).
Conclusion: Pediatric HTN was most often secondary, with renal disease as the leading cause. However, a high proportion of inpatients with unclear type of HTN at discharged, which suggests that careful examination to identify underlying causes is necessary when evaluating pediatric HTN.

关键字 Hypertension; pediatric inpatients; secondary causes.

分类：5. Clinical Epidemiology 临床流行病
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Fat Mass Reverses the Protective Effect of Lean Mass on Cardiovascular Metabolic Factors in Children and Adolescents: Results from the China Child and Adolescent Cardiovascular Health Study

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Background: Despite an increasing number of studies investigating the links between BMI and cardiovascular disease, but these studies cannot accurately assess the influence of fat and muscle mass and their interaction on cardiometabolic abnormalities. In addition, studies indicate that most adipokines are pro-inflammatory and participate in the development of obesity-related metabolic dysfunction, while most muscle factors can counteract the adverse effects of adipokines and have a beneficial effect on glucose and lipid metabolism. This study aims to investigate the associations of body composition compartments, especially the interaction between fat and muscle mass, with cardiometabolic abnormalities in children and adolescents.
Methods: This nationwide cross-sectional study consisted of 8905 children and adolescents (50.1% boys) aged 6 to 18 years who underwent dual-energy x-ray absorptiometry for body composition and had cardiometabolic risk factors measured between January 1, 2013, and December 31, 2015. We calculated fat mass index (FMI), and lean mass index (LMI, bone mineral contents were subtracted). The exploratory outcomes were hypertension, dyslipidemia, hyperglycemia, and insulin resistance. Furthermore, to test the effect of interaction between fat and muscle mass on cardiometabolic abnormalities, we divided children and adolescents into 4 phenotypes: Normal FMI-Normal LMI, Normal FMI-High LMI, High FMI-Normal LMI, and High FMI-High LMI. Multivariable-adjusted linear regression coefficients and ORs were calculated by mixed effect models to assess the associations between body composition indicators and cardiometabolic abnormalities. Hierarchical analysis to study the effect of interaction on the cardiometabolic abnormalities.
Results: In the multivariate model containing FMI and LMI, after adjustment for region, family income, puberty development, physical activity, sedentary activity, drinking alcohol and smoking, unlike FMI, LMI was inversely associated with TC (β: -0.12; 95% CI: -0.16, -0.08), LDL cholesterol (β: -0.06; 95% CI: -0.10, -0.03), and non-HDL cholesterol (β: -0.06; 95% CI: -0.10, -0.02) in boys and TC (β: -0.05; 95% CI: -0.10, -0.01) in girls. Regarding the influence of the interaction between fat and muscle mass on the cardiometabolic abnormalities, taking the High FMI-Normal LMI as the reference group, boys' (with High FMI-High LMI) TG, LDL cholesterol, non-HDL cholesterol has significantly increased 0.18, 0.13, 0.21, separately, and HDL cholesterol have significantly decreased 0.10. Girls' (with High FMI-High LMI) TG have significantly increased 0.11 and HDL cholesterol have significantly decreased 0.09. Analyze for lipid indicators as categorical variables demonstrated similar results.
Conclusions: There are different relationships between body composition compartments and cardiometabolic abnormalities in children: FMI is associated with an increase in the presence of all these factors, while LMI is protectively associated with TC, LDL cholesterol, and non-HDL cholesterol. But, when there is too much fat mass in the body, it will reverse the protective effect of lean mass on cardiovascular metabolic

factors in children and adolescents. Prospective studies are warranted to evaluate the long-term impacts of interaction between fat and muscle mass on cardiovascular risk and further understanding of the mechanism of interaction between fat and lean mass on cardiovascular metabolism is of great significance for the prevention and intervention of cardiovascular and metabolic diseases caused by obesity.

关键字 Fat mass, Lean mass, intercation, Cardiovascular Metabolic Factors, children

分类：5. Clinical Epidemiology 临床流行病
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Impact of the COVID-19 Outbreak on Disease Spectrum in pediatric intensive care unit (PICU)

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Objective: We aimed to analyze the changes of disease spectrum data in pediatric intensive care unit (PICU) during the coronavirus disease 2019 (COVID-19) outbreak and explore the feasible plan for the treatment of critically ill children.
Methods: Patient demographics, distribution of disease spectrum, result of etiological examination and PICU length of stay were compared during the COVID-19 period (2020) and the previous years (2018 and 2019).
Results: The number of PICU admissions in 2020 was 46.8% and 47.8% lower than in 2018 and 2019, respectively. There are significant differences in the number of patients in different age group, and the differences were mainly found in children younger than 4 years old and over 14 years old age group. The proportion of children with respiratory diseases, cardiovascular diseases and accidents decreased significantly, while poisoning and critically diseases partial increased and rare diseases increased significantly. Notably, there was a significant increase in the number of rare diseases categories and the proportion of mitochondrial disease exceeded the autoimmune encephalitis. However, PICU lengths of stay (LOS) in 2020 were higher than in 2018 and 2019 and it indicated that the changes of disease spectrum did not directly affect the LOS. Etiological examination showed bacteria increased and virus decreased.
Conclusions: A striking decrease in PICU admissions was observed during the COVID-19 outbreak, and the disease spectrum changed significantly. Changes in the number and characteristics of children admissions of PICU should be considered to facilitate the effective operation of PICU during the pandemic.

关键字 Coronavirus disease; COVID-19 outbreak; Pediatric intensive care unit; Disease spectrum

分类：5. Clinical Epidemiology 临床流行病
1365

Characteristics of gut microbiota in infants aged 0 to 36 months in Beijing

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Objective To investigate the changes of gut microbiota in infants aged 0 to 36 months and the effects of exclusive breastfeeding before 6 months on the diversity of gut microbiota. **Methods** A multi-center epidemiological study was conducted in Haidian District, Changping District, Shijingshan District and Tongzhou District of Beijing from January 2021 to April 2021. Fresh feces from healthy singleton infants aged 0 to 36 months were collected in Haidian Maternal and Child Health Hospital, Jishuitan Hospital and Luhe Hospital affiliated to Capital Medical University from March to April 2021. A total of 291 infants were selected and divided into 6 groups according to the age of 0 to 3 days, 42 days, 3 months, 6 months, 6 to 12 months and 12 to 36 months. The 16S rRNA V4 region was sequenced using Illumina Novaseq 6000 sequencing platform. In order to analyze the characteristics of gut microbiota changes with age and the effect of feeding style on gut microbiota. **Results** (1) There were significantly differences in the diversity and species composition of gut microbiota among infants in different age groups. With the increase of age, the Shannon index of gut microbiota showed an increasing trend. At the phylum level, the gut microbiota of infants was mainly composed of Proteobacteria, Firmicutes, Actinobacteria and Bacteroidetes. Proteobacteria was the most abundant in newborns, but with the increase of age, Firmicutes gradually replaced Proteobacteria as the main dominant bacteria. (2) Infants who were exclusive breastfed before 6 months had higher Shannon and Observed-otus index after weaning than infants who were continuously breastfed (P=0.015); In currently weaned infants, the Shannon index was higher in infants who were exclusively breastfed than infants who were partial breastfed before 6 months (P=0.011). **Conclusion** The gut microbiota of infants aged 0 to 36 months changed significantly with age, and the diversity and composition of gut microbiota varied significantly in different age groups. Whether exclusive breastfeeding before 6 months had a significant impact on the gut microbiota of infants.

关键字 infant; gut microbiota; High-throughput sequencing; exclusive breastfeeding

分类：5. Clinical Epidemiology 临床流行病
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Sex-specific pattern in blood pressure and cardiovascular structure and its association with birth weight in preschool-aged children

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Background:
Gender-related differences, also called sex dimorphism, in blood pressure and cardiovascular health has been well documented, and it may start in early adolescence, but the data were limited at an early age regarding the sex difference in cardiovascular outcomes and its association with birth weight. Whether the association of macrosomia and cardiovascular outcome influenced by obesity also remains unknown.
Objective:
Based on the data of Shanghai Birth Cohort, we aimed to explore the sex dimorphism of cardiovascular outcomes, including blood pressure and left ventricle (LV) geometry and function, at an early age of 4-year-old. The relationship between birth weight by gender and whether the association was affected by childhood obesity would also be investigated in this study.
Methods:
We recruited 1193 children at 4 years old from the Shanghai Birth Cohort as our subjects. Detailed maternal information and birth weight data are recorded in detail. Blood pressure, echocardiography and anthropometry assessment were conducted for all subjects. Sex difference in anthropometric parameters and LV structure and function were explored. Linear regression models were used to analyze the association between birth weight and LV structure and function changes in each sex category. Multivariable logistic regression models were used to compared risk of undesirable cardiovascular outcome, e.g. left ventricle hypertrophy (LVH), in different birthweight groups, as well as in BMI-stratified birthweight groups by gender.
Results: Compared to girls, boys had higher systolic blood pressure (SBP). The SBP in boys and girls were 99.33±7.88mmHg and 96.75±7.42mmHg, respectively (P＜0.001). Boys showed a higher prevalence of hypertension than girls (P=0.003). Higher left ventricle mass index (LVMI) was also showed in boys (26.96±4.48g/$m^{2.7}$ vs. 25.44±4.92g/$m^{2.7}$, P＜0.001). Boys with macrosomia showed a higher LVMI (β=1.29, 95%CI: 0.14, 2.43), even after adjustment of the maternal and offspring factors. No significant association in girls was found. Compared to normal birth weight groups, boys with macrosomia showed a higher risk of LVH, with an odds ratio of 2.79 (95%CI: 1.17, 6.63, P=0.020), especially in boys with normal BMI. No significant association in girls was found.
Conclusion: In this cross-sectional study, we found that the sex dimorphism did exist in blood pressure and left ventricle structure in preschool aged children. Hypertension were more common in boys than girls. Furthermore, we firstly demonstrated that sex difference in the association with birthweight and cardiovascular outcome and it developed as early as 4 years old.

关键字 sex difference， blood pressure， left ventricular hypertrophy

分类：5. Clinical Epidemiology 临床流行病
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Association of childhood asthma with intra-day and inter-day temperature variability in Shanghai, China

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Objectives: Short-term temperature variability (TV) is associated with the exacerbation of asthma, but little is known about the relative effects of intra- and inter-day TV. We aimed to assess the relative impacts of intra- and inter-day TV on childhood asthma and to explore the modification effects by season.
Methods: A quasi-Poisson generalized linear regression model combined with a distributed lag nonlinear model was adopted to evaluate the nonlinear and lagged effects of TV on childhood asthma in Shanghai from 2009 to 2017. Intra- and inter-day TV was measured with diurnal temperature range (DTR) and temperature changes between neighboring days (TCN), respectively.
Results: Increased DTR was associated with the elevated relative risk (RR) of daily outpatient visits for childhood asthma (DOVCA) in both the whole year (RRlag0-14 for the 99th percentile: 1.264, 95% confidence interval (CI): 1.052, 1.518) and cold season (RRlag0-12 for the 99th percentile: 1.411, 95% CI: 1.053, 1.889). Higher TCN in the warm season was associated with the increased RR of DOVCA (RRlag0-14 for the 99th percentile: 2.964, 95% CI: 1.636, 5.373). The number and fraction of DOVCA attributed to an interquartile range (IQR) increase of TCN were higher than those attributed to DTR in both the whole year period and warm season. However, the number and fraction of DOVCA attributed to an IQR increase of DTR were greater than those attributed to TCN in the cold season.
Conclusions: Our results provide novel evidence that both intra- and inter-day TV might be a trigger of childhood asthma. Higher DTR appeared to have greater impacts on childhood asthma in the cold season while an increase in TCN seemed to have bigger effects in the warm season.

关键字 Asthma, children, temperature variability, relative risk, tailored strategies

Gastroenterology &

Nutriology

消化与营养

Category: 11. Gastroenterology Nutriology 消化与营养
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Intestinal microbiota profiles in infants with acute gastroenteritis caused by Rotavirus and Norovirus infection:a prospective cohort study

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Abstract Content Objective The study was conducted to determine the intestinal microbiota profiles in infants after Rotavirus (RV) and human Norovirus (HNoV) infections, and estimate the potential distinctive species after viral infection.

Methods Fecal specimens from18 infants (11.8 ±3.0 mo.) and 24 infants (8.8 ±6.4 mo.) with acute gastroenteritis caused by RV (G9P8) and HNoV (GII) infection were collected prospectively.The fecal microbiome was assessed by 16S rRNA amplicon pyrosequencing. Alpha diversity, beta diversity, deferentially abundant taxa, and microbial functions were assessed by bioinformatic analysis.

Results The RV group showed higher abundance of Actinobacteria at the phylum level and Bifidobacterium, Streptococcus, Enterococcus, and Lactobacillus at the genus level. The HNoV group showed richness in Fusobacteria and Cyanobacteria at the phylum level and Enterococcus and Streptococcus at the genus level. The Chao1 of HNoV group was higher than control group (P=0.0003), while it was lower in RV group than HNoV group (P=0.0078). Although there was a significant difference in beta diversity between the viral and control groups, no significant difference in beta diversity was observed between the RV and HNoV groups. The genus Bacillus was the characteristic microbiota. Genus Neisseria was effective in distinguishing infected infants (error rate=9.76%, AUC=0.98), while Streptococcus (error rate=12.7%, AUC=0.98) and Pseudomonas (error rate=6.17%, AUC=0.99) were effective in distinguishing healthy infants from those infected with RV and HNoV, respectively. Leptotrichia could be used with a certain accuracy (error rate=20.91%, AUC=0.8) to distinguish RV from HNoV infected infants. Compared with control group, the viral groups (P≤0.01), RV group (P=0.002), and HNoV group (P≤0.01) all showed significant differences in potentially pathogenic bacteria. .

Conclusion There were changes of microbiota structure at phylum and genus levels emerged in infants after RV and HNoV infections. Chao 1 index of alpha diversity increased significantly in HNoV group. Bacillus was detected as the characteristic genus in infected group. Increase of pathogenic bacteria, particular Streptococcus and Enterococcus were detected in infected infants.

Key words intestinal microbiota; rotavirus; human norovirus; infants

Reference

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Antibiotic Resistance of Helicobacter pylori Isolated from Children in Chongqing, China

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Background: The resistance of H. pylori to antibiotics is increasing worldwide and influence severly the eradication rate of H. pylori, the antibiotic resistant rates of H. pylori varies with different geographic areas and times. However, limited studies have reported about the antibiotic resistance and the related gene mutations of children in Chongqing, a city located in southwest China.
Materials and Methods: The 112 H. pylori strains isolated from gastric biopsies of children at Children's Hospital of Chongqing Medical University were collected and resistant rates of these strains to six antibiotics were tested. The A2143G, A2142G mutations in 23S rRNA gene related to clarithromycin resistance and Asn87, Asp91 mutations in gyrA gene related to levofloxacin resistance of isolated 102 strains were investigated.
Results: The resistance rate to clarithromycin, metronidazole, levofloxacin was 47.3% (53/112), 88.4% (99/112), 18.8% (21/112), respectively. No resistance to amoxicillin, tetracycline and furazolidone was observed. Dual, triple resistant percentage was 37.5% (42/112), 10.7% (12/112), respectively. The detection rate of A2143G mutation in 23S rRNA gene was 83.3% (40/48). The detection rates of mutations of Asn87, Asp91 in gyrA gene were 52.6% (10/19) and 36.8% (7/19), respectively.
Conclusions: The prevalence of H. pylori resistance to clarithromycin, metronidazole, levofloxacin from Chongqing children in China was high. The A2143G mutation was detected in most clarithromycin-resistant strains, and Asn87 and Asp91 of gyrA mutation points were common in levofloxacin-resistant strains. These results suggested that the standard triple therapy was not suitable for the eradication of H. pylori in Chongqing children, it’s necessary to explore newer treatment regimens for eradication of H. pylori.

关键字 Helicobacter pylori (H. pylori), antibiotic resistance, children.

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Bleeding from gastric adenomyoma with embedded heterotopic pancreatic tissue in a one-year-old child: A case report

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Background: Bleeding can occur anywhere along the gastrointestinal tract, and identification of the site may be challenging. Heterotopic pancreas is a rare cause of gastrointestinal bleeding in children. This report will show the diagnosis procedure of the bleeding caused by the heterotopic pancreas.
Case presentation: A 1-year-old male who presented with hematochezia. The gastroscopy and endoscopic ultra-sonography demonstrated nodular lesions in the gastric antrum extending to the duodenal bulb. Computed tomogram demonstrated an irregular, linear hyperdense strand in the prepyloric region. Angiography also showed a lesion located near a branch of the superior pancreaticoduodenal artery. Local excision of the lesions was performed, and histopathology of the lesion revealed the concomitant presence of adenomyoma (AM) and heterotopic pancreatic (HP) tissue. The postoperative course and follow-up for 6 months after the surgical procedure were uneventful.
Conclusions: we reported the bleeding caused by the heterotopic pancreas. The endoscope and the endoultrasonogragy were valuable in the diagnosis while the surgry was important in the last diagnosis of the bleeding.

关键字 Adenomyoma, heterotopic pancreas, gastrointestinal bleeding, children

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Food protein-induced enterocolitis:a clinical analysis of 5 cases and literature review

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Objective To summarize and analyze the clinical features of food protein induced enterocolitis syndrome (FPIES), so as to promote clinicians' understanding of the disease. Methods The medical history and follow-up data of 5 children with FPIES diagnosed in Department of Gastroenterology, Beijing Children’s Hospital of Capital Medical University from July 2018 to September 2019 were collected, and their clinical characteristics were summarized and analyzed. Results 5 children with FPIES were all infants， including 3 women and 2 men. Before the onset of the disease, the average number of visits before diagnosis was 3. The departments before diagnosis included multiple departments. There were 4 cases of milk protein allergy and 1 case of egg white allergy. All the patients had acute vomiting [5 cases (100%)], diarrhea [4 cases (80%)], early shock symptoms [5 cases (100%)], transient fever [2 cases (40%)]. Hematogenous leukocytes were increased in 3 cases (60%), CRP was increased in 1 case (20%), faecal leukocytes+[2 case (40%)], occult blood + [1 case (20%)]. Four cases were tested for food allergen specific IgE, of which 2 cases (40%) were positive for milk protein. After avoided allergens, three patients (60%) needed intravenous rehydration treatment, two (40%) received oral rehydration treatment, the disease recovered quickly. Three patients (60%) used antibiotics. Four (80%) of the first-degree relatives of FPIES had a clear history of allergy. Before the diagnosis, the family awareness of FPIES was low. After the diagnosis, strictly avoided the allergen according to the doctor's instructions, and no similar allergic reaction occurred again. Under the guidance of the doctor, they gradually added supplementary food, two patients had multiple food allergies. The body weight and length of two children with growth retardation were catching up with each other. Conclusions FPIES is a serious food allergy related gastrointestinal disease which is easy to be misdiagnosed clinically. The diagnosis needs to integrate the family and personal allergy history, diet records, the characteristic performance of disease onset, the effect of diet avoidance and carry out necessary differential diagnosis. The long-term management and monitoring after diagnosis is also very important.

关键字 Food protein induced enterocolitis syndrome; Milk protein; Egg white; Children

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Individually Designed Fully Covered Self-Expandable Metal Stents for Refractory Benign Esophageal Strictures: Ten-years' Experience with Chinese Pediatric Patients

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Background: At present, there are neither clear guidelines for the treatment of refractory benign esophageal strictures (RBESs) with an esophageal stent nor specific esophageal stents designed for children. This study aimed to share our institutional experience of placing individually designed fully covered self-expandable metal stents (FCSEMSs) for the treatment of RBESs in pediatric patients.
Methods: A 10-year retrospective study between May 2009 and July 2020 that includes 14 children with RBESs who were treated with individually designed FCSEMSs. Patients were followed-up regularly after stent placement to observe the improvement of vomiting and dysphagia, changes in stenosis diameter and complications.
Results: A total of 20 stents were successfully placed in 14 patients (eight males and six females: age range 4 to 11 years). During a follow-up period ranging from 5 to 83 months, except for one 4-year-old child who could not endure chest pain, the remaining 13 patients all benefited from stenting. Their Ogilvie & Atkinson scores improved from grade III-IV to grade 0-I, and the diameters of the stenosis were enlarged from 2-5 mm to 9-14 mm. Two patients developed restenosis and granulation tissue hyperplasia was found in 2 patients, stent migration and malapposition occurred in 2 patients with esophageal perforations, which required further endoscopic intervention.
Conclusions: The use of FCSEMS for RBES is safe and effective in selected pediatric patients. Rationally designed stents and timely management of postoperative complications are critical to ensure the success of this new method.

关键字 esophageal stenosis; stents; children; endoscopy

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A unique swelling lesion in esophagus

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Objective To discuss the importance and necessity of digestive endoscopy and preoperative imaging examination for the diagnosis and treatment of digestive foreign body in children.

Methods In this paper, we report a 4-year-old girl child with progressive dysphagia. The course of the disease was 1 month, and no clear history of foreign body ingestion was provided. Chest CT and initial gastroscopy showed a swelling lesion in the esophagus, and space-occupying lesions were considered, but histopathology did not support it. Through the efforts of the gastroenterology doctors in Xi'an Children's Hospital, it was clear that the esophageal swelling lesions were granulation tissue hyperplasia and embedded formation caused by foreign body incarceration for a long time.Endoscopic removal of foreign bodies in the digestive tract is minimally invasive, fast recovery and less damage, which is the preferred treatment for foreign bodies in the digestive tract. However, the patient has abundant blood supply to the peripheral tissues of esophageal foreign bodies, endoscopic operation is quiet difficult, prone to bleeding and perforation.After preoperative multidisciplinary consultation, the consensus was that the best choice is endoscopic foreign body removal surgery in the operating room, and make preparations for thoracic surgery at any time. The surgeon used a hook knife to cut through the locally proliferated granulation tissue gradually and radially. Finally, the upper edge of the foreign body was separated and exposed. Under the Olympus H-290, the guide wire was inserted into the gap between esophageal wall and foreign body. And the foreign body forcep was again inserted through the cavity of the foreign body tube, clamped the guide wire, and slowly pulled the foreign body to loosen at the original incarceration place. after our endeavor, the foreign body was successfully removed (Figure 5).When bilateral pneumothorax and esophageal perforation occurred in the child during the operation, thoracic closed drainage was immediately performed, a 16mm×80mm film-covered recoverable esophageal stent was placed to block the perforation of the esophagus, and a gastric tube was placed.

Results However, due to the prolonged incarceration of foreign body, secondary esophageal stenosis and obvious mucosal hyperplasia around the narrow mouth were found. Therefore, endoscopic balloon dilatation of esophageal stenosis and radial resection of esophageal stenosis were performed repeatedly in our hospital on a regular basis.the child now eats normally through the mouth with no vomiting and dysphagia, and the endoscopic (Olympus H290) was successfully passed, and she is well in growth and development.

Conclusion Esophageal foreign body incarceration is the common cause of acquired esophageal stricture.

Therefore, for the patients with uncertain history of foreign body ingestion, or foreign body incarceration for too long, or high risk of bleeding and perforation, we should carefully discern radiography image and endoscopic changes, and choose minimally invasive treatments as far as possible, try to avoid unnecessary traditional surgery in other words trying our best to solve problems for children with minimal risk. At the same time, preoperative multi-disciplinary consultation is required to assess the surgical risks, and it is crucial to be prepared and ready to resort to the thoracic surgery at any time during endoscopic surgery when something occurred made it necessary, so as to ensure the life safety of the children.

关键字 swelling lesion, foreign body, esophageal stenosis

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Gastric Peroral Endoscopic Pyloromyotomy for in Infants with Congenital Hypertrophic Pyloric Stenosis: The First Multicentre Study

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Objective: Congenital hypertrophic pyloric stenosis (CHPS), the most common disease requiring surgery in infants, is routinely treated with open or laparoscopic pyloromyotomy. However, repeated vomiting may retard or suspend infant growth, rendering the infant unable to tolerate surgery. Gastric peroral endoscopic pyloromyotomy (G-POEM), an innovative, minimally invasive technique based on POEM, has been implemented to treat CHPS. This study evaluated the efficacy and safety of G-POEM in treating CHPS.
Design: The data of 21 CHPS patients treated with G-POEM from January 2019 to December 2020 at four advanced children's endoscopic medical centres in China were reviewed. Data regarding basic information, surgical procedures, perioperative management, complications and follow-up outcomes were summarized.
Results: The median operative duration was 50 (23-150) mins, and the median hospitalization duration was 13 (9-26) days. Eight patients had intraoperative complications, including 5 cases of mucosal injury, 2 cases of tunnel disorientation and 1 case of an insufficiently tight mucosal seal. Eight patients had postoperative complications, including 5 cases of vomiting, 1 case of diarrhoea, and 2 cases of transfer to the intensive care unit. All complications were successfully managed. The median follow-up duration was 13 (3-19) months after surgery. The median weight was increased by 0.92 (0.0-1.6) kg at one month and 3.2 (2.6～3.5) kg at three months.
Conclusion: G-POEM could be safely performed in infants with CHPS, with effective clinical responses over short-term follow-up. Further multicentre studies should be performed to compare this technique with open or laparoscopic pyloromyotomy over long-term follow-up.

关键字 Gastric Peroral Endoscopic Pyloromyotomy，Congenital Hypertrophic Pyloric Stenosis，treatment，multicentre Study

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Endoscopic radial incision for benign esophageal strictures in children

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Objective To evaluate the efficacy and safety of endoscopic radial incision (ERI) for benign esophageal strictures in children. Methods The clinical data of 20 children with esophageal stenosis treated by ERI during the period of January 2013 -December 2018 were reviewed. The operation, improvement of clinical symptoms, and complications related to the operation were summarized. Results All of the 20 cases were successfully treated with ERI. Operation time: 5-25 minutes, average 10 minutes. Narrow ring incision was performed for 1-8 times, average 4 times. No fever, poststernal pain, bleeding and perforation were found in all children after operation. Length of hospitalization: 4-7 days, average 4.5 days. Postoperative follow-up was 3-24 months, average 7.9 months. At one month after operation, the stenosis was enlarged in all the 20 cases ($P<0.001$) and dysphagia score was lower than that before operation($P<0.001$). The dysphagia score at three months after operation were the same as that at one months after operation. The weight gain of 19 children increased after three months by 1-4kg, average 2.0kg. There was no significant correlation between the improvement of dysphagia after ERI and sex, age, times of preoperative treatment and diameter of stenosis (all $P > 0.05$), but there was a negative correlation between the improvement of dysphagia after ERI and the length of the stenosis area ($P < 0.05$). Conclusion ERI is safe and effective in the treatment of benign esophageal strictures in children, and is worthy of clinical promotion.

关键字 Esophageal stenosis, benign; Child; Endoscopic radial incision; Efficiency efficacy Safety

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MicroRNAs as Potential Biomarkers for the Diagnosis of Inflammatory Bowel Disease: A Systematic Review and Meta-analysis

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Background and Aim: The clinical significance of aberrantly expressed microRNAs (miRNAs) in diagnosing inflammatory bowel disease (IBD) has not been well established. We aimed to investigate the clinical diagnostic value and the role of miRNAs in the pathogenesis of IBD by a systematic review and meta-analysis.
Methods: We retrieved published articles from the online databases including PubMed, EMBASE, Web of Science, and the Cochrane Library from inception to March 17, 2021. We used a random-effects meta-analysis to obtain sensitivity, specificity, positive (PLRs) and negative likelihood ratios (NLRs), diagnostic odds ratio (DOR) and area under the curve (AUC) with 95% CIs for the diagnosis of IBD.
Results: A total of 117 studies reporting altered miRNA expression in IBD were initially included in the systematic review. Among them, 15 studies involving 613 IBD patients and 22 miRNAs and 2 miRNA panels were finally eligible for meta-analysis. Pooled analyses showed a moderate diagnostic accuracy of miRNAs in distinguishing IBD from the other subjects, with a sensitivity of 0.80 (95% CI: 0.79-0.82), a specificity of 0.84 (95% CI: 0.82-0.86), a DOR of 21.19 (95% CI: 13.90-32.31) and an AUC of 0.89. Subgroup analyses revealed better performance for ulcerative colitis patients (AUC=0.93) than Crohn's disease patients (AUC=0.84), for distinguishing IBD from healthy controls (AUC= 0.90) than non-IBD controls (AUC= 0.80). Consistent upregulation of miR-21, miR-16 and miR-192 in blood with a high-moderate diagnostic accuracy was found in at least two studies.
Conclusions: The findings suggest that miRNAs could be credible diagnostic biomarkers in IBD.

关键字 MicroRNA，Inflammatory Bowel Disease，Potential Biomarkers，Diagnosis，A Systematic Review and Meta-analysis

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The influence of Helicobacter pylori eradication on Intestinal metaplasia of gastric mucosa in children

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Aim
Probe into the feature of the Intestinal metaplasia of gastric mucosa and effect of Helicobacter pylori eradication.

Methods
The subjects were 54 children who underwent gastroscopic biopsy of gastric mucosa, whose pathological tissue showed intestinal metaplasia and Helicobacter pylori (Hp) was successfully eradicated. Observing the Gastroscopy and gastric mucosal specimens’ pathological changes under light microscope by using Rapid urease test (RUT) and HE staining, PAS staining and HP methylene blue staining, two of the three (RUT, histopathological examination or UBT) are positive means clinical diagnosis of HP infection.4 weeks to 2months after the eradication therapy and Hp eradication can be conformed if UBT, gastroscopy and pathological examination were showed negative.

Results
There were 54 cases of intestinal metaplasia of gastric mucosa, from which we can mainly observe the goblet cells and absorptive intestinal epithelium and especially the former, Pan's cell also common in it. The degree of intestinal metaplasia was mainly mild of 39 cases, the cases of moderate intestinal metaplasia and severe intestinal metaplasia are 12 and 3. Reexamine after eradication Hp, among the 5 cases, 1 case of moderate intestinal metaplasia and 4 cases of the mild. Meanwhile, Intestinal metaplasia in children was clearly improved.

Discussion
Atrophy and intestinal metaplasia of gastric mucosa may induce the gastric cancer. There is a lack of evidence can be showed that intestinal metaplasia of gastric mucosa can cause HP infection in children at present. Effect of eradication of Hp infection on intestinal metaplasia of gastric mucosa in children are also in needed. Some adult cases suggested the detection rate of HP in patients with intestinal metaplasia of gastric mucosa is higher than that in patients without it. Hp infection, as the main factor, is closely related to intestinal metaplasia of gastric mucosa. Though many researches have been taken but no evidence can ensure whether intestinal metaplasia can be reversed after Hp eradication, some people in China believe that intestinal metaplasia disappeared and the rate of reduction can reach 45.8% after 6 months of follow-up after Hp eradication, it has also been reported abroad that 61% can achieve recovering after 2 years of follow-up. This research shows that intestinal metaplasia in children is significantly improved after Hp eradication. The researches in worldwide shows that the eradication of HP cannot reverse the intestinal metaplasia. With the increase of age and the persistence of inflammatory factors (HP infection), its intestinal metaplasia will be difficult to reverse. It will be significant to understand and prevent the causes and occurrence of irreversible intestinal metaplasia and even gastric adenocarcinoma in adulthood if we take research and treatment of HP infection and gastritis with intestinal metaplasia in minors seriously.

关键字 Helicobacter pylori，Intestinal metaplasia，children

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Fructooligosaccharides Promotes Intestinal Barrier Function by Strengthening the Epithelium and Modulating Gut Microbiota in Food Allergy

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Objective: The present study aimed to decipher the protective effects of Fructooligosaccharides on the intestinal epithelium and microbiota as well as the effects of modulated microbiota on epithelial function, identify individual or group gut microbes relating to food-allergy and intestinal permeability. Method: Intestinal permeability was measured by Urinary levels of lactulose (L) and mannitol (M) and the L/M ratio in egg-allergic mice. The structures of gap junctions, tight junctions and desmosomes and mast cells were observed by transmission electron microscopy. Gene and protein expression levels of tight junction (TJ) proteins and cytokines were determined by qRT-PCR, ELISA. Fecal microbiota composition in children and mice was assessed by 16S-rDNA. Result: The results showed that FOS improved intestinal epithelial permeability. Furthermore, FOS increased the level of TGF-β and IL-10. Importantly, FOS modulated the gut microbiota, individual gut microbes may be related to food-allergy and intestinal permeability. Conclusion: Taken together, these findings indicated that FOS could positively regulate the gut microbiota, increased levels of TGF-β and IL-10, improved intestinal epithelial permeability.

关键字 Fructooligosaccharides； Intestinal Barrier Function； Gut Microbiota； Food Allergy

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Clinical characteristics of gastrointestinal bleeding in infants

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Abstract: Objective: To investigate the etiology and clinical characteristics of gastrointestinal hemorrhage in infants. Methods: Clinical data of 207 infants with gastrointestinal bleeding admitted to the Department of Gastroenterology from January 1, 2016 to December 31, 2018 were retrospectively analyzed to summarize their etiology and clinical characteristics. The data were processed by SPSS25.0 statistical software, and the measurement data were expressed as mean ± standard deviation (x± s), while the counting data were expressed as percentages (%). Results: Among the 207 cases of gastrointestinal hemorrhage, 121 cases are male and 86 cases are female, with an average age of 4.60±3.05 months (range from 1 month to 11months). Symptoms include hematemesis in 40 cases (19.32%), vomiting coffee grounds in 4 cases (1.93%), melea in 4 cases (1.93%) and hematochezia in 160 cases (77.30%). The main cases of hematochezia are small infants and large infants, and the main cases of hematemesis are infants less than 7 months old. Among the 207 infants with gastrointestinal bleeding, most of them are little infants with 98 cases (47.34%). The bleeding site is mainly lower gastrointestinal bleeding with 161 cases (77.78%), and the upper gastrointestinal bleeding with 46 cases (22.22%) is relatively less. Cow’s milk protein allergy is the most common cause in 129 cases (62.32%), followed by bacterial enteritis in 45 cases (21.74%). The main cause of gastrointestinal bleeding in infants under 7 months of age is cow’s milk protein allergy, and bacterial enteritis was the most common cause in 33 cases (15.94%) of older infants. Meckel's diverticulum was concentrated in older infants. The average course of disease is 16.6±28.4 days, and the longest course of disease is anal fissure (58.0±79.7 days), while the shortest is Meckel's diverticulum (1.8±1.1 days), and the decrease of hemoglobin (69.4±6.3 g/L) in Meckel's diverticulum is the most obvious. The course of disease in infants with cow’s milk protein allergy is 20.6±30.0 days, and some of them (12.40%) are accompanied by diarrhea. Infants with bacterial enteritis have a course of disease with 5.5±6.5 days, most of them (73.33%) are accompanied by fever and diarrhea, and a few of them (26.67%) only have diarrhea. 45 infantile cases with bacterial enteritis are mainly Salmonella infection, of which 26 cases are Salmonella typhimurium serotype (26/45, 57.78%). Conclusions: Gastrointestinal bleeding was most common in infants aged 1-3 months, mainly in lower gastrointestinal bleeding. Among the causes, cow’s milk protein allergy was the most common disease, and cow’s milk protein allergy was considered first in infants with hematemesis or hematochezia. Bacterial enteritis was given priority to stool blood in older infants. Meckel's diverticulum should be considered first in patients with short course and significant hemoglobin decrease.

关键字 Infant, Gastrointestinal bleeding, Etiology, Clinical manifestations

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Susceptibility analysis of the Vitamin A and E in children with diarrhea

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Abstract: Objective: Analyze the association between the children with diarrhea and vitamin A/E. Methods: To investigate the levels of the vitamin A and E in children with diarrhea, we compared blood samples from 96 diarrhea patients (diarrhea group) and 91 normal controls (control group) by High Performance Liquid Chromatography-MS/MS (HPLC-MS/MS) during the September 2017 and August 2019. The general data was used the SPSS 25.0 statistical software to analyse, the measuring data used t test, counting data used percentage (%), ranked data used Z test, and the Pearson correlation analysis was used to analyze the association between the children with diarrhea and vitamin A/E. Results: Compared the serum levels of vitamin A and E in the two groups of children, the diarrhea group was lower than the control group ($t=13.45$, 9.42, $P < 0.01$). Children with diarrhea and serum level of vitamin A/E were negative correlation with Pearson correlation analysis ($r = 0.703$, 0.569, $P < 0.01$). The levels of vitamin E in children with virus infection was lower than the children with bacteria infection significantly ($F=5.48$, $P<0.01$). Conclusions: The serum levels of vitamin A and vitamin E in children with diarrhea were significantly reduced. Children should be given supplemental vitamin A and E to avoid diarrhea, especially the children with virus infection.

关键字 Children; Diarrhea; Vitamin A; Vitamin E

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Early diagnosis of children with Wilson's disease in southern China by using common clinical parameters, a cross-sectional retrospective analysis

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Aims: Development of early diagnostic criteria for Wilson's disease (WD) in children by using ALT (alanine aminotransferase) elevation as the first symptom.
Methods: A cross-sectional retrospective analysis of the clinical data and genetic test results of children with WD in southern China in the past four years, and the follow-up study of their short-term prognosis.
Results: Thirty children with elevated ALT as the first manifestation of WD in southern China were enrolled in this study, including 14 females and 16 males. The patients were diagnosed at 2 years to 11 years and 4 months, with an average age of 5.08±2.06 years. Among them, liver enzymes of 30 cases (100%) were found to be elevated in physical examination. Specifically, in all the 30 cases (100%), serum ceruloplasmin (CP) level was decreased, whereas the 24-hour urinary copper excretion volume was increased. However, no changes in the basal ganglia, thalamus and brainstem were detected in 12 cases by head Magnetic Resonance Imaging (MRI). Furthermore, the ATP7B gene containing 65 allelic mutations were detected from all the 30 patients, including 51 missense mutations (78.4%), 5 nonsense mutations (7.6%), 4 synonymous mutations (6.1%), 4 frame-shift mutations (6.1%) and 1 mutation at splice junction (1.5%). Generally, a total of 15 (23.0%) hot spot mutations, p.R778L, were documented. In particular, the two mutation sites c.2333G>T and c.3443T>C have the highest mutation frequency, accounting for 23.0% and 10.7% of the total number of mutation sites, respectively. Subsequently, the telephone-based follow-up was carried out from 1 month to 4 years and 2 months after diagnosis for all the 30 patients. In detail, 2 cases were lost contact, and 27 cases were successfully recovered, whereas 1 patient died because of acute liver failure.
Conclusions: Early diagnosis and treatment of WD will substantially increase the survival rate and have good prognosis. And this early diagnosis in children could be done quickly by referring to three parameters including elevated ALT, decreased ceruloplasmin level and increased 24-hour urinary copper. This diagnostic standard can be applied in routine physical examination, together with negative result from head MRI examination and no neurological manifestations. The genetic mutation test of ATP7B gene is used to confirm the diagnosis eventually.

关键字 Children, southern China, hepatolenticular degeneration, clinical features, genetic mutation.

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RNA splicing, a versatile regulatory mechanism in paediatric liver diseases

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With the development of high-throughput sequencing technology, the post-transcriptional mechanism of alternative splicing is further understood. From decades of studies, alternative splicing is discovered to occur in multiple tissues including brain, heart, testis, skeletal muscle and liver. And it may play an important role in physiological functions and most of liver diseases. In particular, as the increasingly incidence rate of non-alcoholic fatty liver disease (NAFLD) worldwide, which is in parallel with obesity, NAFLD has become the most common and fundamental liver disease towards the development of severe liver damage or cancer. Furthermore, the progress of disease is accelerated in children, leading to severe damage of their liver tissue if no precautions have been taken. To this end, this review article summarizes the recent studies of alternative splicing in liver diseases, paying special attention to liver damages in children. The discussion of the regulatory role of splicing in liver diseases and their potential as new therapeutic targets has been carried out as well.

关键字 Alternative splicing, Liver disease, Non-alcoholic fatty liver disease, RNA sequencing, Splicing factor, Children

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The role of Genus Megamonas, Species of Megamonas hypermegale and Megamonas rupellensis in the gut microbiota of nonalcoholic fatty liver disease in children and adolescents

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Background and Aim: Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in children and adolescents. Gut microbiota plays a role in the pathophysiology of NAFLD through the gut-liver axis. So, we aim to know the genus and species of gut microbiota and their functions in children and adolescents with NAFLD.
Material and methods: 58 children and adolescents were enrolled in this study, including 27 abnormal weight (AW) (obese) with NAFLD patients, 16 AW non-NAFLD children and 15 healthy children. All of them underwent magnetic resonance spectroscopy (MRS) to quantify the liver fat fraction. Stool samples were collected and analyzed with metagenomics. We used MetaPhlAn2 for enhanced metagenomic taxonomic profiling and HUMAnN2 for functional annotations. The differences between groups in taxonomic composition and function annotations were determined using Kruskal-Wallis test. Beta diversity was calculated based on Jaccard index. Wilcoxon Rank-Sum test or Kruskal-Wallis test were used for diversity differential analysis.
Result: According to body mass index (BMI) and MRS proton density fat fraction (MRS-PDFF), we divided the participants into BMI groups including AW group (n=43) and Lean group (n=15), MRS groups including NAFLD group (n=27) and Control group (n=31), and BMI-MRS 3groups including NAFLD_AW (AW children with NAFLD) (n=27), Ctrl_AW (n=16) (AW children without NAFLD) and Ctrl_Lean (n=15). There was no difference in gender and age among those groups ($p>0.05$). The age, BMI and MRS-PDFF were not normally distributed (shapiro test, $p< 0.05$), while the BIM and MRS-PDFF was significant correlation (Spearman's rho = 0.7). In BMI groups, within genus level, Dialister, Akkermansia, Odoribacter and Alisstipes exhibited a significant decrease in AW children, compared with Lean group. At species level, Megamonas hypermegale was increased in AW group, while Akkermansia muciniphila, Dialister invisus, Alistipes putredinis, Bacteroides massiliensis, Odoribacter splanchnicus and Bacteroides thetaiotaomicron were decreased in AW children, compared to the Lean group. Between MRS groups, the Genus Megamonas and the species of Megamonas hypermegale and Megamonas rupellensis were increased in NAFLD group, compared with Control group. Among the BMI-MRS 3groups, the Genus Megamonas was enriched in NAFLD_AW group, while Odoribacter, Alistipes, Dialister and Akkermansia were not abundant, compared with Ctrl_Lean or Ctrl_AW group at genus level. Megamonas hypermegale and Megamonas rupellensis exhibited a significant increase in NAFLD_AW children, compared with Ctrl_Lean or Ctrl_AW group at species level. In other words, Megamonas hypermegale and Megamonas rupellensis were abundant in obese children with NAFLD, but not in obese children without NAFLD. Compared with healthy children, the pathways contributed by Genus Megamonas were significantly increased in AW children with NAFLD.
Conclusions: We found that the Genus Megamonas was enriched at genus level of children with NAFLD, while Megamonas hypermegale and Megamonas rupellensis were enriched at species level in children with NAFLD, the latter two species were not abundant in obese children without NAFLD. Therefore, the Genus Megamonas, species of

Megamonas hypermegale and Megamonas rupellensis in the gut microbiota may be underlying or in part of the pathogenesis of NAFLD.

关键字 Megamonas, Gut microbiota, Nonalcoholic fatty liver disease, Children

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The twists and turns of diagnosis and treatment of pediatric Neuro-Behcet’s disease: a case report and literature review

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Neurological manifestations in a patient with Behcet’s disease (BD) led to the identification of Neuro-Behcet’s disease (NBD). As there is no specific diagnostic test, the diagnosis and management of NBD is challenging. We report a 11-year and 11-month boy who underwent right eye intraocular lens implantation, appendectomy, perianal abscess removal, thalidomide therapy and infusions of infliximab for his Crohn disease (CD). Enhanced Magnetic Resonance Imaging (MRI) and Magnetic Resonance Venography (MRV) were performed to address the onset of headache during the course of his treatment which showed Cerebral Venous Sinus Thrombosis (CVST). After the diagnosis of NBD, he was treated with thrombolysis, anticoagulation, and low-dose hormone combined with immunosuppressant (cyclophosphamide), leading to his recovery. Here, we describe how NBD is prone to misdiagnosis and missed diagnosis, and should be diagnosed based on the clinical manifestations, colonoscopy, pathological examination and MRI or MRV.

关键字 Neuro-Behcet's disease, Child, Cerebral Venous Sinus Thrombosis, Diagnosis

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Two novel mutations in the SKIV2L gene associated with Syndromic Diarrhea, or Trichohepatoenteric Syndrome: a case report and literature review

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Background: Syndromic Diarrhea (SD) or Trichohepatoenteric Syndrome (THES) is an autosomal recessive inherited disease leading to intractable diarrhea, which is associated with the mutation of superkiller viralicidic activity 2-like (SKIV2L) gene or tetratricopeptide repeat domain-containing protein 37(TTC37) gene. The patient of SD or THES in China or in the world is uncommon.
Case presentation: We report the case of a one-month and fourteen-day-old female infant who was admitted for diarrhea and failure to thrive that began after she was born. Those basic examinations showed no obvious abnormality, including blood routine, C-reactive protein, etiological testing of stool, liver function, renal function, thyroid function, abdominal ultrasound and so on. So, after approval from the clinical research ethics committee and informed consent was obtained, we chose whole exome sequencing to identify the mutations in this patient. As a result, two heterozygous mutations in the SKIV2L gene, c.3602_3609delAGCGCCTG (p.Q1201Rfs*2) and c.1990A>G (p.T664A) were identified and confirmed by Sanger sequencing, which were the novel mutations without reported. After having an amino acid formula feeding from less to more pumped continuously through a gastric tube and supplemented with a parenteral nutrition, this patient got better with a decrease in stool frequency.Conclusions: We experienced a novel case with the mutations in the SKIV2L gene that caused SD or THES, which provides valuable experience for clinic, although there are still no specific methods to treat it.

关键字 Syndromic Diarrhea, Trichohepatoenteric Syndrome, SKIV2L, Diarrhea

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Hepatitis B virus surface antigen titers at 10 years of age predict the risk of advanced liver fibrosis in adulthood

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Abstract Content Hepatitis B virus (HBV) surface antigen (HBsAg) is a surrogate markers of HBV covalently closed circular DNA (cccDNA). We aimed to elucidate the relationship between the baseline HBsAg titer in the early phase of chronic HBV infection on the progression of liver fibrosis in adulthood in this study.

Methods We recruited 214 initially hepatitis B e antigen-positive chronic HBV infected patients (122 males) followed since 8.44 ± 0.26 till 38.21 ± 0.37 years of age in this study. Serum HBsAg titers were assessed in the serum samples collected at 10, and 15 years of age.

Results During the 6,371 person-years follow-up period, 11 subjects (5.14%) developed METAVIR F3-4 liver fibrosis at their 4th decade of life. Both the HBsAg titers at 10 and 15 years of age are correlated with the spontaneous HBeAg-seroconversion and HBsAg-seroclearance. Subjects with METAVIR F3-4 liver fibrosis were noted to have more genotype C HBV infection, higher HBsAg titers at their 10 and 15 years of age ($P = 0.003$, <0.001, and <0.001, respectively). The ROC curve analysis identified the cutoff of HBsAg > 4.23 and > 4.44 log10 IU/mL at 10 and 15 years of age, respectively, for the best prediction of METAVIR F3-4 liver fibrosis at their 4th decade of life ($P = 0.001$ and < 0.001, respectively).

Conclusion The HBsAg titers at childhood, indicating the baseline cccDNA and integrated HBV genomes, predict the progression of liver fibrosis in adulthood.

Key words covalently closed circular DNA, hepatitis B core-related antigen, hepatitis B surface antigen, liver stiffness measurement, transient elastography

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Clinic investigation of the children with simple obesity in Guangzhou revealed the potential cardiac dysfunction

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Cardiovascular disease is a leading cause of morbidity and mortality worldwide. The incidence of cardiovascular disease at a younger age is closely related to childhood obesity. Childhood obesity, as one of the potential risk factors of cardiovascular diseases, has been increasing with the rapid development of economy in China. Its potential impact on the cardiovascular system of children has become one of the concerns of healthy growth. Here, we study the cardiovascular aspects of 79 obesity children and 161 normal weight children in Guangzhou. Compared to normal weight children, Obesity group did not show significant difference on age, gender ratio, born weight, born length, percentage of puberty, parents' BMI and other baseline characteristics, but significant different on weight percentage of medium($P < 0.0001$), height percentage of medium($P=0.0007$), age and sex adjusted BMI($P < 0.0001$), waist circumference($P < 0.0001$) and WHR($P < 0.0001$). Obesity group have higher blood TG level($P=0.0001$), TC level($P=0.0070$), LDL-C level($P < 0.0001$), LDL-C/HDL-C level($P < 0.0001$) and lower HDL-C level($P < 0.0001$) than the normal children. significantly higher level of CK, LHD, s-Flt-1 in obesity group ($P=0.0062$, $P=0.0012$, $P=0.0013$) indicate the potential Myocardial damage markers. Oxidation index like hs-CRP and UA were higher in obesity group than healthy group ($P=0.0225$ and $P<0.0001$) indicate the higher risk of cardiovascular event. cardiac function investigation shows that not only higher diastolic blood pressure($P=0.0074$), heart rate($P=0.0049$) in obesity children, but also 52.4% obesity children were described overall declination of left and/or right ventricular function through Color Doppler echocardiography. There were significant differences between obesity and healthy group on IVSd, LVPWD and AO ($P< 0.0001$, $P=0.0003$ and $P< 0.0001$). Therefore, our Analysis based the children in Guangzhou revealed that the high risk for cardiovascular disease and the potential cardiac dysfunction in children with simple obesity.

关键字 children; simple obesity; clinic investigation; cardiovascular dysfunction; Guangzhou

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Use of body composition and phase angle analysis for the assessment of nutritional status and clinical outcomes in critically ill children

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We aimed to investigate the efficiency of bioelectrical impedance analysis (BIA) measurements and phase angle (PhA) analysis for the assessment of nutritional risk and clinical outcomes in critically ill children.This single-center observational study included patients admitted to the Pediatric Intensive Care Unit (PICU) of Chengdu Women’s and Children’s Central Hospital. All patients underwent anthropometric measurement in the first 24 h of admission and underwent BIA measurements within 3 days after the admission. The patients were classified into different groups based on body mass index (BMI) for age. Electronic hospital medical records were reviewed to collect clinical data for each patient. All the obtained data were analyzed by the statistics method.There were 204 patients enrolled in our study, of which 32.4% were diagnosed with malnutrition. We found that BMI, arm muscle circumference, fat mass, and %body fat were lower in the group with poorer nutritional status (P<0.05). Evident differences in the score of the Pediatric Risk of Mortality and the duration of mechanical ventilation (MV) among the three groups with different nutritional statuses were observed (P<0.05). Patients in the severely malnourished group had the longest duration of MV. In the MV groups, there were significant differences (P<0.05) in albumin level, PhA, and extracellular water/total body water (ECW/TBW ratio). The ECW/TBW ratio and the time for PICU stay had a weak degree of correlation (Pearson correlation coefficient = 0.375). PhA showed a weak degree of correlation with the duration time of medical ventilation (coefficient of correlation = 0.398).
Conclusion: BIA can be considered an alternative way to assess nutritional status in critically ill children. ECW/TBW ratio and PhA were correlated with PICU stay and duration time of medical ventilation, respectively.

关键字 bioimpedance analysis; phase angle; critical illness; nutritional assessment; prognosis; children

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Amino-acid-abandonment strategy-based new Lactobacillus plantarum membrane proteins (LpMPs) and their TLR4/TGF-β/Smad-associated anti-colitis activities

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Background & Aim 1: Inflammatory bowel disease (IBD), a group of idiopathic chronic colorectal diseases with a progressive and unpredictable course, can impede living aspirations and impair quality of life in patients. The incidence and prevalence of IBD is increasing globally even though it was traditionally regarded as a disease of the western world. IBD has already become a global burden. Children with very early-onset inflammatory bowel disease (VEO-IBD) represent a distinct group of patients with IBD with unique phenotypic and genetic characteristics. As at now, therapeutic strategies for the management of the disease are limited. There is an urgent need to innovate treatment strategies against (VEO-)IBD and to develop new anti-colitis drugs to overcome these limitations of existing therapies.

Background & Aim 2: In recent years, the use of probiotic agents has become a new strategy. Results from our previous studies indicated that *Lactobacillus plantarum*, a common probiotic, exhibits therapeutic effects against IBD, and through screening, we further obtained an active 61-amino-acid long protein, *L. plantarum* membrane protein 1 (LpMP-1). The number of amino acids in an ideal druggable peptide should generally be less than 50; a greater molecular weight leads to higher incidence of adverse reactions, probably due to increased immunogenicity, and this is disadvantageous in terms of druggability and clinical application. Based on druggability-guided strategies, the search for LpMPs with lower molecular weights and better bioactivities is necessary.

Methods: Herein, we used amino-acid-abandonment strategies to obtain modified LpMPs (LpMP-2 - LpMP-9) using LpMP-1 as the parent template. Furthermore, we systematically evaluated the anti-colitis pharmacodynamics of these LpMPs in terms of symptomatology, histopathology, and cytokine levels in dextran sulfate sodium (DSS)-induced colitis mice. Treatment strategies of colitis mice were: (i) LpMP-1 with doses of 5, 50, 500 μg/kg, and cyclosporin A (CsA) with 10 mg/kg (ip, n = 8); (ii) LpMP-1 with 50 μg/kg, aluminum hydroxide with 0.28 g/kg, and the combination of the two (ig, n = 8); (iii) LpMP-1 - LpMP-9 with 50 μg/kg, and CsA with 10 mg/kg (ig, n = 8); and (iv) LpMP-8 with doses of 5, 50, 500 μg/kg, LpMP-1 with 50 μg/kg, and CsA with 10 mg/kg (ig, n = 8). Using the DSS-induced colitis model, we next analyzed colonic proteomics by iTRAQ-based liquid chromatography tandem mass spectrometry (LC-MS/MS) in the different treated mouse groups; after that, we established interested LpMP-structures by non-homologous computational simulation, and carried out protein-protein docking between LpMPs and interested targets. Then, we discussed their relationships at the molecular and cellular levels through the biotin-based ELISA system, LPS-treated FACS assay, and (semi-)quantitative characterization of colitis-related proteins and cytokines. We aimed to investigate LpMPs' possible mechanism of action against IBD under an iTRAQ-based pharmacoproteomic system and a docking-guided receptor-ligand relationship frame.

Results: We found a new active protein, LpMP-8, which had a lower molecular weight than LpMP-1. LpMP-8 was found to exhibit anti-colitis activity following oral

administration in vivo (50 μg/kg) by improving symptoms of colitis, colonic ulcerations, and cytokine disorders. iTRAQ-based pharmacoproteomic analysis revealed that TLRs and TGF-β were involved in the mechanism of LpMP-8 against colitis; docking-guided receptor-ligand relationships suggested that LpMP-8 competes with TLR4-MD2-bound LPS and to reverse TLR4/TGF-β/Smad pathway disorders.
Conclusion: Overall, our probiotic-derived LpMP-8 was shown to elicit anti-colitis activity following oral administration, and its significant efficacy is probably associated with the TLR4-MD2/TGF-β/Smad pathway.

关键字 inflammatory bowel disease; Lactobacillus plantarum membrane proteins (LpMPs); amino-acid-abandonment strategies; anti-colitis; TLR4-MD2; TGF-β/Smad

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RNA-sequencing identifies novel transcriptomic signatures in parenteral nutrition-associated liver disease

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Background. Total parenteral nutrition (TPN) dependence leads to development of parenteral nutrition-associated liver disease (PNALD). The spectrum of diseases ranges from cholestasis, steatosis, fibrosis, and cirrhosis that causes significant morbidity. Understanding the disease at molecular level helps us to develop therapeutic targets. We performed transcriptomic analysis on liver from rats with TPN administration, and we assessed the role of selected differentially expressed genes (DEGs), functional pathways, transcriptional factors, and their associations with pathological parameters of PNALD.
Methods. Sprague-Dawley rats were subjected to TPN or standard chow with 0.9% saline for 7 days as controls. RNA-seq analysis was performed on liver samples. Correlations between transcriptional factor hairy and enhancer of split 6 (Hes6) and pathological parameters of PNALD were investigated.
Results. We provided a comprehensive transcriptomic analysis to identify DEGs and functional pathways in liver from PNALD rats. We identified solute carrier family 7 member 11 (*Slc7a11*) as the most up-regulated mRNA, and ferroptosis-associated pathways were enriched in PNALD rats. Transcriptional factor (TF) analysis revealed that Hes6 interacted with Nr1d1, Tfdp2, Zbtb20, and Hmgb2l1. TF target gene prediction analysis suggested that Hes6 may regulate genes associated with bile acid secretion and fatty acid metabolism. Last, hepatic *Hes6* expression was significantly decreased in PNALD rats, and was positively correlated with several taurine-conjugated bile acids and negatively correlated with hepatic triglyceride level.
Conclusions. RNA-seq analysis revealed unique transcriptomic signatures in the liver following TPN administration. Hes6 may be a critical regulator for PNALD pathogenesis.

关键字 parenteral nutrition, transcriptomics, Hes6, bile acids, metabolome

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Pediococcus pentosaceus CECT 8330 attenuates DSS-induced colitis by regulating the intestinal microbiota and immune responses

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Abstract
Background: Compelling evidences demonstrated that gut microbiota dysbiosis plays a critical role in the pathogenesis of inflammatory bowel diseases (IBD). Treatments for targeting the microbiota may provide alternative options for the treatment of IBD, such as probiotics. Here, we aimed to investigate the protective effect and involved mechanisms of a probiotic strain, Pediococcus pentosaceus (P. pentosaceus) CECT 8330, on dextran sulfate sodium (DSS)-induced colitis in mice.
Methods: Female C57BL/6 mice were administered phosphate-buffered saline or P. pentosaceus CECT 8330 (5×108 CFU/day) once daily by gavage for 5 days prior to colitis induced by DSS. Weight, fecal conditions, colon length and histopathological changes were examined. ELISA and flow cytometry were applied to determine the cytokines and regulatory T cells (Treg). Western blot was used to examine the tight junction proteins in colonic tissues. Fecal short-chain fatty acids (SCFAs) levels and microbiota composition were analyzed by targeted metabolomics and 16S rRNA gene sequencing, respectively.
Results: P. pentosaceus CECT 8330 treatment alleviated DSS-induced colitis as evidenced by improving the weight loss, disease activity index (DAI) score, histological damage, and colon length shortening. P. pentosaceus CECT 8330 decreased the serum levels of proinflammatory cytokines (TNF-α, IL-1β, and IL-6), and increased levels of IL-10 in DSS treated mice. P. pentosaceus CECT 8330 upregulated the expression of ZO-1, Occludin and the ratio of Treg cells in colon tissue. P. pentosaceus CECT 8330 increased the fecal SCFAs level and abundance of protective genera, including norank_f_Muribaculaceae, Lactobacillus, Bifidobacterium, and Dubosiella, which were positively correlated with IL-10 and SCFAs levels, and negatively associated with IL-6, IL-1β, and TNF-α, respectively.

Conclusion: P. pentosaceus CECT 8330 administration attenuates the DSS-induced colitis by protecting the gut barrier function, and restoring the dominant gut bacteria genera and SCFAs that modulate immunological profiles. Therefore, P. pentosaceus CECT 8330 may serve as a promising probiotic to ameliorate intestinal inflammation.

关键字 Pediococcus pentosaceus, probiotic, colitis, gut microbiota, IBD

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Nutrition Support and Weight Growth Velocity in Premature Infants

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Background & Objective: Insufficient nutrition intake in premature infants remains a common issue. This study aimed to assess the association between weight gain and nutrition intake in premature infants during hospitalization.Methods: This prospective study was performed in Xinhua Hospital from February 2017 to June 2019. Overall, 501 premature infants were enrolled in this study. Nutrition support was provided according to the “CSPEN guidelines for nutrition support in neonates”. Infants were divided into the following four groups according to their birth weights (BWs): group A (BW ≥ 2,500 g), B (2,000 ≤ BW < 2,500 g), C (1,500 ≤ BW < 1,500 g), and D (BW < 1,500 g). The nutrition intake and growth velocity (GV) were analyzed in these groups. We also divided infants into five groups according to the parenteral nutrition (PN) energy ratio of total energy: group 1 (80% < PN ratio ≤ 100%), group 2 (60% < PN ratio ≤ 80%), group 3 (40% < PN ratio ≤ 60%), group 4 (20% < PN ratio ≤ 40%), group 5 (0 < PN ratio ≤ 20%). The standard value was 105 kcal/kg/d. Nutrition intake and GV were analyzed in these groups.
Results: The highest average total energy intake and GV of very low birth weight infants (VLBWIs) were 104.5 ± 10.9 kcal/kg/d (P < 0.001) and 10.8 ± 2.2 g/kg/d (P < 0.001), respectively. In group 3, the average enteral nutrition (EN), total energy intake, and GV values were 28.0 (19.4–36.7) kcal/kg/d, 81.8 (72.6–90.8) kcal/kg/d, and 1.0 ± 12.4 g/kg/d, respectively. In group 5, the average EN, total energy intake, and GV values were 96.4 (81.6–103.2) kcal/kg/d, 114.3 (99.2–123.5) kcal/kg/d, and 9.9 (2.1–16.9) g/kg/d, respectively.
Conclusion: The energy intake and growth velocity were the highest in VLBWIs. The decrease in PN was much faster than EN advance in group 3, while the growth velocity was the lowest. Therefore, we should consider maintaining an increased EN when reducing PN in premature infants.

关键字 nutrition support, parenteral nutrition, enteral nutrition, growth velocity, premature infants

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Effects on liver function of children with intestinal failure in three different lipids

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Objectives: MCT/LCT fat emulsion, fish oil-based lipid emulsion and multi-oil-based lipid emulsion are the current three choices for parenteral nutrition support of children in China. Focused on the main complication , the aim of this study was to compare the alteration of liver function during the application of PN, and assess the difference among three initial lipid strategies.
Methods: A retrospective clinical study comparing MCT/LCT lipid and fish oil-based lipid and multi-oil-based lipid (SMOFlipid). Patients with Intestine Failure (IF) on parenteral nutrition (PN) for at least 2 weeks were enrolled into our study, the main indexes for observation were liver indicators (TBA, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (AKP), gamma glutamyl transferase (γ-GT), total bilirubin (TB), or direct bilirubin (DB)).
Results: 144 in-patients participated in our study (62 MCT/LCT lipid, 50 SMOFlipid and 32 fish oil lipid). Levels of TBA, ALT, AST, AKP, γ-GT showed no significant difference during SMOFlipid therapy (P>0.1). With MCT/LCT lipid therapy, levels of ALT, AST, AKP, γ-GT significantly increased from 44.00 (range 23.50-81.00 U/L) to 90.00 (range 45.50-143.00 U/L; p=0.000), 63.00 (range 44.25-84.50 U/L) to 80.50 (range 44.00-120.00 U/L; p=0.003), 233.00 (range 160.50-325.70 U/L) to 268.00 (range 196.50-386.50 U/L; p=0.008), 78.50 (range 17.25-141.75 U/L) to 100.50 (range 36.25-214.63 U/L; p=0.003) respectively. In fish oil (FO) group, levels of ALT, AST, γ-GT significantly decreased from 128.00 (range 82.00-255.00 U/L) to 99.00 (range 51.00-174.00 U/L; p=0.004), 110.00 (range 92.00-193.00 U/L) to 84.00 (range 59.00-169.00 U/L; p=0.008), 161.00 (range 113.00-292.00 U/L) to 136.00 (range 82.00-211.00 U/L; p=0.027) respectively. Among groups, we compared the differences between PN therapy before and after (values after the calculation of liver indicators after PN therapy delete those numbers before PN). The alleviation of ALT, AST in FO group showed significance compared to the other two groups(P<0.05), the elevation of γ-GT level in SMOF group was significantly lower than MCT/LCT group (P=0.01), and it did not differ between SMOF group and FO group (p=1.00).
Conclusions: Compared with MCT/LCT lipid, SMOFlipid seems to reduces the risk of progressive liver damage in children with intestinal failure while fish oil lipid significantly alleviates the liver injury in children.

关键字 Liver function; Lipid emulsion

分类：11. Gastroenterology Nutriology 消化与营养
1010

Predictive Value of Insulin-like Growth Factor 1 Standard Deviation Score on the Risk of Non-alcoholic Fatty Liver Disease in Obese Children

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Objective To evaluate the predictive value of insulin-like growth factor Ⅰ standard deviation score (IGF-ⅠSDS) on the risk of non-alcoholic fatty liver disease (NAFLD) in obese children.**Methods** In this retrospective study, we collected the anthrometric and clinical biochemical indexes in 179 hospitalized children diagnosed as obesity who had been examined by abdominal ultrasound. The patients were divided into four groups according to the quartile of IGF-ⅠSDS:group 1 (＜P25), group 2 (P25~P50), group 3 (P50~P75) and group 4 (≥P75).The correlation between IGF-ⅠSDS and clinial indexes was analyzed.The risk factors of NAFLD were assessed by logistics regression analysis and the predictive value of IGF-ⅠSDS was evaluated by the area under the receive operating characteristic curve. **Results** A total of 179 obese children were included in this study, aged from 5.0 to 15.5 years old. 139 obese children were male and 40 were females. 90 obese children were diagnosed as fatty liver. A significantly greater BMI and systolic blood pressure, and higher levels of fasting C-peptide, 2-hour plasma insulin, ALT, GGT, triglyceride, uric acid ,prevalence of puberty and prevalence of fatty liver, but a lower level of growth hormone were found in patients in group 1 than the other 3 groups. IGF-ⅠSDS showed a positive correlation with growth hormone (r=0.194,P=0.01) and a negative correlation with ALT (r=-0.16,P=0.42). The difference was statistically significant. Multivariate logistic analysis demonstrated that HDL-C (OR 0.214,95% Cl 0.048~0.956,P=0.043), IGF-ⅠSDS (OR 0.735,95% Cl 0.543~0.995,P=0.047) were risk factors of NAFLD in obese children. The area under the ROC of NAFLD for IGF-ⅠSDS in obese children was 0.5966（95%Cl 0.5137~0.6796，P=0.0256）,with a sensitivity of 35.56% and a specifity of 85.39%. **Conclusions** The level of IGF-ⅠSDS is associated with NAFLD in obese children, which can predict the risk of NAFLD in obese children.

关键字 Non-alcoholic fatty liver disease; Children; Insulin-like growth factor Ⅰ; Obesity

分类：11. Gastroenterology Nutriology 消化与营养
1047

Efficacies of phenotype-guided therapy versus genotype-guided therapy based on clarithromycin resistance for Helicobacter pylori infection in Chinese children

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Background: Clarithromycin resistance reduced the eradication rate of empirical triple therapy and sequential therapy with Helicobacter pylori (H pylori). Culture with susceptibility test and molecular determination of genotype were recommended to guide tailored therapy. Our primary aim is to investigate whether the eradication rate of the phenotype-guided therapy and genotype-guided therapy based on clarithromycin resistance can achieve above 90% in Chinese children.

Methods: We retrospectively enrolled H pylori infected patients (aged between 6 and 18 years old) who underwent endoscopy and agreed to undergo both culture and genetic test for clarithromycin resistance. Patients receiving tailored therapy based on traditional culture results (phenotype-guided therapy) or genetic testing results (genotype-guided therapy) were finally included in the study. The success of eradication was evaluated by a 13C-urea breath test (UBT) or by upper GI endoscopyby with RUT and histology at least 4 weeks after the completion of treatment. The primary endpoint was the eradication frequency of H pylori in the full analysis set (FAS), which included all children who received at least one dose of the treatment and with available follow-up data.

Result: Between September 2017 and October 2020, 226 eligible patients with follow-up data performed both biopsy culture and molecular testing. 71 patients with clarithromycin-susceptible strains were in phenotype-guided therapy group and 87 patients without 23S rRNA point mutation (A2142G, A2142C and A2143G) were in genotype-guided therapy. The eradication rates were 70.4% for phenotype-guided therapy (50/71, [95% CI: 59.5%-81.3%] and 92.0% for genotype-guided therapy (80/87, [95%CI: 86.1%-97.8%]). The cure rate was significantly higher in the latter group (P<0.01). The incidence of side effects was 4.2% (3/71) and 10.3% (9/87) following phenotype-guided therapy and genotype-guided therapy with no major differences between groups (P=0.15). The compliance rates was similar between the two groups (97.2% vs 95.4%, p=0.87).

Conclusion: Tailored therapy according to the genetic testing results achieved eradication rates of 92% and was superior to tailored therapy by traditional culture‐based tests.

关键字： Helicobacter pylori; tailored therapy; clarithromycin; phenotype; genotype

分类：11. Gastroenterology Nutriology 消化与营养
1049

Safety and feasibility of ketogenic diet for children with febrile infection-related epilepsy syndrome complicated with super refractory status epilepticus

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Objective: To investigate the safety and feasibility of ketogenic diet (KD) for children with febrile infection-related epilepsy syndrome (FIRES) complicated with super refractory status epilepticus (SRSE).
Methods: The clinical data of 18 patients with FIRES complicated with SRSE treated by KD in the intensive care unit (ICU) of Children's Hospital of Fudan University from April 2015 to March 2021 were analyzed retrospectively. All patients adopted a fasting initiation scheme (fasting time ≤ 72 hours). Ketogenic formula (2:1～4:1) was given by nasal tube (NG) feeding based on the peripheral blood ketone level, gastrointestinal tolerance, and nutritional status of the patients. Peripheral blood ketone and blood glucose were monitored daily. Liver and kidney function, electrolyte, and trace elements were monitored regularly to check whether the children had side effects, such as hypoglycemia, gastrointestinal intolerance, hypoproteinemia, and hyperlipidemia in the KD initiating phase (2 weeks) and KD stabilization period (> 2 weeks).
Results: A total of 18 patients were included, including 9 males, aged (7.3 ± 0.7) years, and the interval from fever onset to the first attack was (0 ~ 6) days. All patients started KD after ineffective treatment with anesthetics combined with a variety of antiepileptic drugs, and 3 patients received vagus nerve stimulation combined with KD. Among the 18 patients, 4 cases stopped the treatment because of inefficacy in the stabilization stage of KD, 1 case stopped the treatment because of the withdrawal care. 1 case had a 37-days course of KD, then developed severe hyperlipidemia. After reducing the proportion of KD, the blood lipid level was not improved and the ketogenic effect was not significant, so KD was stopped. 66.7% (12 / 18) of patients were effective in KD treatment, and the effective ratio was 2.2:1 ~ 4:1. Among them, 10 cases were transferred to the department of neurology for continued treatment after maintaining KD for (30.0 ±19.1) days. After 124 days of treatment in ICU, 1 effective patient was transferred to the local hospital for further treatment; 1 case was treated for 38 days and KD was effective, KD treatment was stopped because of arrhythmia and renal calculi. During the initiating phase of KD, 27.8% of the patients had hypoglycemia, 27.8% of the patients had gastrointestinal adverse reactions, 61.1% of the patients had hypoproteinemia, 77.8% of the patients had hypercholesterolemia, and 61.1% of the patients had hypertriglyceridemia. With adjusting the proportion of KD, adjusting the amount of formula, and adding ketogenic protein powder and other nutritional treatment measures, the above adverse reactions were improved in the stable stage of KD treatment.
Conclusion: The ketogenic diet is an effective treatment for children with FIRES complicated with SRSE. Most of the early common adverse reactions are temporary, and close monitoring does not affect the implementation of KD. KD is safety and feasibility.

关键字 ketogenic diet, febrile infection-related epilepsy syndrome, super refractory status epilepticus

分类：11. Gastroenterology Nutriology 消化与营养
1057

The association between genetic variants, pharmacokinetics and infliximab efficacy in Chinese pediatric Crohn’s disease

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Background Infliximab is an effective therapy for inducing and maintaining remission in patients with Crohn's disease (CD). Early noninvasive predictors of disease remission allow infliximab treatment modifications. The aim of this study was to investigate the associations between genetic variants, pharmacokinetics and infliximab efficacy in pediatric patients with CD.

Methods This retrospective observational study included CD patients under at least 14 weeks of infliximab therapy between August 2015 and December 2020. All patients were biologic naïve. Clinical evaluation was performed before induction treatment and at week 0, 14, 30 and 54 of IFX therapy by weighted Pediatric Crohn’s Disease Activity Index (wPCDAI) with cut-off values for clinical remission (<12.5 points, CR). Colonoscopy was performed before EEN/corticosteroids induction therapy, at week 0 and 30 of IFX therapy. Mucosal healing (MH) was defined as the Simple Endoscopic Score for Crohn disease (SES-CD) <3 points. Demographics, laboratory tests, medication data and disease activity index were collected. TLI and ATI were measured at week 14 and reactive drug monitoring was performed during follow-up. 10 single nucleotide polymorphisms involved in the NF-κB mediated inflammatory response, pharmacokinetics and therapeutic response to infliximab were genotyped.

Results A total of 62 pediatric CD patients met the eligible criteria. The median duration of IFX treatment was 20.1 months (IQR 12.6-29.87). Clinical remission (CR) rate was 69.4% and 63.2% at week 14 and week 30, respectively. Among 49 patients who underwent endoscopic reexamination at week 30, MH was observed in 30.6% of patients. At week 54, 66.7% of patients (32/48) achieved CR. In univariate logistic regression analysis, white blood cell, erythrocyte sedimentation rate and wPCDAI before IFX initiation were significantly associated with CR at week14. TLI was associated with CR at week 14, and MH at week 30 (both P=0.002). However, the association was lost between TLI and CR at week 54 (P=0.188). The multivariate logistic regression analysis confirmed that TLI at week 14 was significantly independently associated with the CR at week 14 and MH at week 30 (P=0.007 and P=0.025, respectively). ROC curves showed that the optimal TLI threshold level capable to distinguish between CR group and non-CR group at week 14 was 2.62 μg/mL with an AUROC of 0.79 (P<0.001, sensitivity 69.2%, specificity 78.9%). Furthermore, the threshold value of TLI at week 14 capable to differentiate patients with or without MH at week 30 was 3.34 μg/mL with an AUROC of 0.85 (P<0.001, sensitivity 78.6%, specificity 79.4%). No significant differences in CR or MH rate in the first year were found based on SNP genotype. ATI level was below the detection limit (< 4 ng/ml) among the 74.2% (46/62) of patients at week 14. As the IFX treatment progressed, 16 of 62 patients (25.8%) showed positively increased antibody levels (defined as ATI >30 ng/ml). The median time from the inception to ATI detection in our population was 13.48 months (IQR 8.57-23.02). In the time-to-event analysis, TNFRSF1B CC genotype (rs3397) was predictive of significantly earlier ATI occurrence than the TC or TT genotype with the P value < 0.001. The probability of remaining antibody-free three years after the start of IFX therapy was more than 50% in patients with TC or TT genotype. Moreover, compared with patients carrying rs3804099 TC and CC genotype, the patients carrying

rs3804099 TT genotype had lower median TLI (3.7 vs 2.1 μg/mL, P=0.039) and serum TNF-α level (239.0 vs 71.8 pg/ml, P=0.034) at week 14.
Conclusions Higher TLI contributed to achieving MH. Genotyping rs3397 in TNFRSF1B may identify patients who are prone to generate immunogenicity to drugs.

关键字 Crohn′s disease, infliximab, children, single nucleotide polymorphisms, pharmacokinetics

分类：11. Gastroenterology Nutriology 消化与营养
1059

Effects of nutritional status on short-term clinical outcomes in children with umbilical cord blood stem cell transplantation

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Objective: To evaluate the effect of nutritional status of inpatient on short-term clinical outcomes in children with umbilical cord blood stem cell transplantation.
Methods: Clinical data of children who with umbilical cord blood stem cell transplantation were retrospectively collected from January 2019 to December 2020 in the transplantation ward of Hematology Department, Children's Hospital of Fudan University, including primary disease, general conditions, laboratory data, duration of parenteral nutrition(PN), time of granulocyte implantation, time of platelet implantation, pneumonia, sepsis, and graft versus host disease (GVHD). Weight loss ≥7% during hospitalization was defined as high weight loss group (H), weight loss <7% as low weight loss group (L). Nutritional status, clinical characteristics of inpatient in the two groups were annalyzed.
Results: A total of 91 children were included, including 32 cases of primary early-onset inflammatory bowel disease, 51 cases of primary immune deficiency disease, and 8 cases of inborn errors of metabolism. 78 were male and 13 were female. The median age was 1.33 (0.8-3.64) years. Length of stay were 77.9±36.8 days. 61 effective transplantation cases and 28 death cases in total. There were 24 cases in H group and 67 cases in L group. The age of H group 3.55 (1.89, 7.55) years was older than the L group 1.2(0.85, 2.80) (P<0.001). The incidence of skin GVHD in group H(75%) was higher than in group L (47.8%) (P=0.021)). The incidence of intestinal GVHD in group H(37.5%) was higher than that in group L (13.4%) (P=0.015). The length of stay in group H (95.5±34.7 days) was longer than that in group L (71.7±35.7 days) (P=0.006). The hospitalization cost of group H (392,000±185,000 yuan) was higher than that of group L (296,000±113,000 yuan)(P=0.004). Antibiotics cost more (98,000± 58,000 yuan vs 74,000±25,000 yuan, P=0.008). However, there were no significant difference of the time of granulocyte implantation, Platelet implantation time, PN usage time, pneumonia incidence and septicemia incidence in the two groups.
Conclusion: Excessive weight loss during transplantation increases the hospitalazation and cost of inpatient, and is associated with a high incidence of GVHD, which will affect the overall prognosis of transplantation and increases the consumption of medical resources. So nutritional intervention should be carried out as soon as possible for children with weight loss, especially for those older children.

关键字 umbilical cord blood stem cell transplantation; nutritional status; clinical outcomes

分类：11. Gastroenterology Nutriology 消化与营养
1304

Distribution and influencing factors of the sialic acid content in the breast milk of preterm mothers at different stages

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Background & Aims: This study aims to detect breast milk sialic acid (SA) content and the change rule, understand each stage breastfeeding SA secretion and the influence factors of the human milk SA content.
Methods: We recruited mothers and their infants as our subjects. At day 7, 14, 30, 120 and 365 after delivery, the contents of SA in breast milk were collected and detected through Fluorescence Detector-High Performance Liquid Chromatography. The participants completed baseline questionnaire at ≤day7 and were followed up at day 30, 120 and 365.
Results: A total of 95 mothers with 122 infants were included in the analysis, including 22 mothers with 22 term infants, 25 mothers with 35 late preterm infants, 31 mothers with 39 very preterm infants, and 17 mothers with 26 extremely preterm infants. The results of study showed that, compared with breast milk of term mothers at the same period, breast milk of preterm mothers contained more SA at each time node, and the content of SA in breast milk increased with decreasing gestational weeks. Moreover, maternal age, pre-pregnancy BMI, and delivery mode had significant effects on total SA in breast milk especially for the preterm infant breast milk. Significant negative associations occurred between SA contents and infant growth status, especially in preterm infants.
Conclusions: With the prolongation of lactation time, the content of SA in breast milk gradually decreased, and the content of SA in the breast milk of preterm mothers was higher than that of term mothers. In addition, SA content was associated with maternal age, pre-pregnancy BMI, and delivery mode. Moreover, high levels of SA in breast milk were useful for the catch-up growth of preterm infants.

关键字 Human milk; Sialic acid; Infant feeding; Lactation period; Preterm infants

分类：11. Gastroenterology Nutriology 消化与营养
1313

Long term follow-up for pediatric intestinal pseudo-obstruction patients in China

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Background: Pediatric intestinal pseudo-obstruction (PIPO) is a heterogeneous and severe group of disorders, and rates of morbidity and mortality remain high. PIPO patients often need long-term nutrition support and may develop malnutrition. The aim of this study was to follow up the nutrition status in PIPO patients.
Methods: Fifty-eight PIPO patients were followed up at least 3 months in Xinhua Hospital, affiliated to School of Medicine, Shanghai Jiao Tong University from January 2008 to May 2020. Patients were diagnosed of PIPO based on ESPGHAN consensus. Data of clinical characteristics, medical and surgical managements, nutrition support, serum vitamins and mineral elements concentrations were collected. The patients were divided into early onset PIPO (EO-PIPO, neonatal onset PIPO) group or later onset PIPO (LO-PIPO, infants or children onset PIPO) group, and follow-up was scheduled every 3 months.
Results: The follow-up duration was 37.8±33.0 months. Total survival rate was 63.8% (37/58), which was 48.5% (17/35) in EO-PIPO group and 87.0% (20/23) in LO-PIPO group, the mortality in EO-PIPO group was higher than in LO-PIPO group (p=0.002). Twenty-one patients died, in which 18 patients (85.7%,18/21) were onset from neonatal period, and 14 patients (66.7%,14/21) died under one year old. Infection was the major reasons of death. Ten patients in EO-PIPO group and 7 patients in LO-PIPO occurred CRBSI, and there was no difference between EO-PIPO group and LO-PIPO group (p=0.879). Twenty-five patients (43.1%,25/58) were severe malnutrition at baseline, and 6 patients (16.2%,6/37) during follow-up. Eight patients (29.6%,8/27) were zinc deficiency, and 7 patients (26.9%,7/26) were vitamin D deficiency at first admission and 5 patients (26.3%,5/19) were zinc deficiency and 10 patients (52.6%,10/19) were vitamin D deficiency during follow-up. Patients who had25-hydroxyvitamin D deficiency at baseline had higher rate of CRBSI (p=0.048) during hospitalization.
Conclusion: Patients with PIPO often develop malnutrition. Early-onset and CRBSI were the high risk for mortality.25-hydroxyvitamin D deficiency patients had higher rate of CRBSI.Zinc and vitamin D deficiencies were common during follow-up and additional supplement were recommended.

关键字 Chronic intestinal pseudo-obstruction; Children; Parenteral nutrition; Micronutrients

分类：11. Gastroenterology Nutriology 消化与营养
1314

Cadherin-11 contributes to cholestatic liver fibrosis via TGF-β/Smad signaling pathway

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Objective: Cadherin-11(CDH11), a cell-to-cell adhesion molecule, is implicated in various biological functions. Biliary atresia (BA) is a common cholestatic liver disease in children and characterized by obliteration of the intrahepatic and the extrahepatic biliary duct, progressive liver fibrosis, and cholestasis. This study aimed to explore the functions of CDH11 in cholestatic liver fibrosis.

Methods: The wild type (*Wt*) and Cdh11 knockout (*Cdh11*$^{-/-}$) mice were subjected to bile duct ligation (BDL) to induce cholestatic liver fibrosis. The extent of liver injury as well as fibrosis and activation of TGF-β/Smad pathway were evaluated. The effect of *CDH11* on the activation of hepatic stellate cell (HSC) line LX-2 cells was investigated. The expression of *CDH11* in BA livers was evaluated.

Results: BDL-induced liver injury and fibrosis were attenuated in *Cdh11*$^{-/-}$ mice compared to *Wt* mice. The protein expression levels of phosphorylated Smad2/3 were decreased in livers of *Cdh11*$^{-/-}$ BDL mice compared to *Wt* BDL mice. *CDH11* knockdown inhibited the activation of LX-2 cells. The expression levels of *CDH11* were significantly increased in livers of BA. *CDH11* was correlated with liver fibrosis in BA.

Conclusion: CDH11 may promote cholestatic liver fibrosis by activating TGF-β/Smad pathway and may act as a potential therapeutic strategy for cholestatic liver disease, such as BA.

关键字 cadherin-11, cholestatic liver fibrosis, hepatic stellate cell, TGF-β/Smad

分类：11. Gastroenterology Nutriology 消化与营养
1318

Mechanism of Overexpressing LncRNA-BC090353 on Cholestatic Liver Injury

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Objective: Cholestasis is caused by obstruction or disruption of bile production and the intracellular retention of toxic bile components like bile salts. If left untreated, cholestasis can lead to fibrosis and cirrhosis, eventually leading to liver failure and need for a liver transplant. LncRNA plays an important role in diverse physiological and pathological processes. The abnormal expression of many lncRNAs is closely related to the occurrence and poor prognosis of various diseases, including hepatocellular carcinoma and biliary atresia liver fibrosis. The biological function and molecular mechanism of lncRNA-BC090353 in cholestatic liver injury remain unclear. Therefore, we investigated the role and mechanism of lncRNA-BC090353 in cholestatic liver injury, providing new ideas and targets for clinical intervention of cholestatic liver disease.

Methods: A total of 29 male Sprague-Dawley rats weighing 100-120 g were randomly divided into 4 groups (each group, n = 4-6): sham + Control AAV9 vector (Sham-CTL), sham+AAV9-BC090353 (Sham-BC090353), BDL+Control AAV9 (BDL-CTL), and BDL+AAV9-BC090353 (BDL-BC090353). For overexpressing lncRNA-BC090353 in the livers of rats, the rattish cDNA was subcloned into the adeno-associated virus serotype 9 (AAV9) transfer plasmid and transfected into HEK293T cells to produce AAV9-BC090353 vector genomes. A dose of 1.0 × 1011 vector genomes of the AAV9-H19 or AAV9 controls were injected into rats via the tail vein. Seven days post-injection, all rats were subjected to either BDL or sham operation. Two weeks after, liver tissues and serum were harvested for further research. Serum transaminase, bile acid and bilirubin levels were detected by biochemical kits. Hematoxylin-eosin, Masson and Sirius red staining were used to observe the level of liver injury and fibrosis. Protein expression levels of TNF α, CD11b, Collagen I, α-SMA, CK19, IL6, P-STAT3 and STAT3 in rats liver were detected by western blot.

Results: We found that BDL up-regulated the expression of lncRNA-BC090353 in rat liver. Overexpression of lncRNA-BC090353 significantly increased BDL-induced liver injury as indicated by the enlarging serum aspartate aminotransferase (AST), γ-glutamyltransferase (GGT), total bilirubin (TBil), and direct bilirubin (DBil). Also, lncRNA-BC090353 reinforced liver fibrosis and cholangiocyte proliferation in cholestatic livers. Histologically, hematoxylin-eosin (H&E) staining revealed that the liver necrosis was induced by BDL. Masson's trichrome and Sirius red staining indicated that the infusion of lncRNA-BC090353 can aggravate liver fibrosis induced by BDL. The mRNA levels of the marker gene for liver fibrosis, Acta2 and Col1a1 increased in BDL-BC090353 rats compared with BDL-CTL rats (Fig). In addition, the western blotting analysis showed that protein levels of both collagenⅠ, α-SMA and cholangiocyte proliferation marker CK19 increased markedly in BDL rat livers. The increase was more pronounced in the BDL-BC090353 group. LncRNA-BC090353 altered the levels of IL6/STAT3 signaling. Phosphorylation of STAT3 was high after the injection of BC090353, p-STAT3/STAT3 increased in BDL-BC090353 rats compared with BDL-CTL rats. The mRNA level of IL6 increased significantly by the injection of BC090353 after BDL, however, the protein level of IL6 was induced by BDL to increase but didn’t show

much difference between BDL-CTL and BDL-BC090353. Key genes MMP7 downstream of IL6 controlling epithelial-mesenchymal transformation were also upregulated, but the difference was not significant.
Conclusions: LncrNA-BC090353 plays an important role in cholestatic liver injury, partly through IL6/STAT3 pathway.

关键字 Long noncoding RNA, BC090353, liver fibrosis, biliary hyperplasia

分类：11. Gastroenterology Nutriology 消化与营养
1319

Inositol hexaphosphate promotes intestinal adaptation in short bowel syndrome

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Background & aims: Short bowel syndrome (SBS) is one of the most common causes of intestinal failure. Promoting intestinal adaptation is critical for decreasing morbidity and mortality in patients with SBS. Dietary inositol hexaphosphate (IP6) plays an important role in maintaining intestinal homeostasis. Here, we reported the beneficial effect of IP6 in a rat model with SBS and clarify the underlying mechanism.
Methods: Forty 4-week-old male Sprague-Dawley rats were divided randomly into the following 4 groups (n = 10 per group): Sham group, Sham+IP6 group, SBS group, and SBS+IP6 group. Rats in the SBS group and SBS+IP6 group received 75% small bowel resection (include the small bowel from 10 cm distal to the ligament of Treitz to 15 cm proximal to the ileocecal valve). Rats in the Sham group and Sham+IP6 underwent bowel transection and re-anastomosed without resection. Rats were administered with IP6 by oral gavage (2.0 mg/g daily) in the Sham+IP6 group and SBS+IP6 group. Rats were sacrificed on day 14 after operation. The intestinal length was measured. Levels of Inositol 1,4,5, -trisphosphate (IP3) were detected using an enzyme-linked immunosorbent assay. Rat small intestinal epithelium cell line (IEC-6) was used to explore the role of IP3.
Results: IP6 treatment promoted intestinal adaptation of SBS rats. The residual intestine and colon were longer in the SBS + IP6 group compared with the SBS group. IP6 treatment resulted in of the proximal small intestine, the distal small intestine, and the colon. Histological staining showed an obvious increase in villus height, crypt depth, and muscle thickness in both the proximal and distal small intestine in the SBS + IP6 group compared to the SBS group. Compared with the SBS group, the mRNA expression levels of Gcg in the residual intestinal mucosa and concentrations of GLP-2 in the serum were increased in the SBS+IP6 group. Additionally, IP6 treatment increased the proliferation of intestinal epithelial cells. The proportion of Ki67-positive cells per crypt was increased in the SBS+IP6 group compared to the SBS group. Consistently, the mRNA expression levels of Lgr5 and Pcna were markedly increased in the SBS + IP6 group compared to the SBS group. IP6 treatment could reduce the concentration of fluorescein isothiocyanate-labeled dextran with a molecular weight of 4,000 Daltons in the plasma of rats in the SBS+IP6 group by 45% compared to rats in the SBS group. Higher levels of IP3 were detected in the feces and serum in IP6-treated SBS rats, suggesting that IP6 could be metabolized into IP3 in the intestine. In vitro, the proliferation of IEC-6 cells was accelerated following IP3 treatment in a dose-dependent manner, and a significant growth-promoting effect was observed when the cells were treated with IP3 at a concentration of 1 μM. Additionally, the Cell Counting Kit-8 (CCK-8) assay showed that absorbance signal increased quickly by 24 hours in the IP3-treated group compared to the unstimulated (IEC-6 cells alone) time-matched controls. Results of the EdU incorporation assay showed that quiescent IEC-6 cells incubated with 1 μM IP3 for 24 hours caused a distinct increase in the incorporation of EdU compared to the control group
Conclusion: IP6 treatment promotes intestinal adaption and may represent a potential therapeutic approach for patients with SBS.

关键字 Inositol hexaphosphate, short bowel syndrome, intestinal adaptation

分类：11. Gastroenterology Nutriology 消化与营养
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Intestinal continuity alleviates pediatric intestinal failure-associated liver disease

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Background and Aim: When ileostomy or jejunostomy are performed after resecting the intestine for necrotizing enterocolitis (NEC) or intestinal atresia, it is called type I short bowel syndrome (SBS). This condition requires long-term parenteral nutrition (PN) and is often accompanied with intestinal failure-associated liver disease (IFALD). This study aimed to observe the impact of intestinal continuity on the hepatic function of pediatric intestinal failure (IF) patients with type I SBS.
Methods: The pre-and post-anastomosis medical records of 35 pediatric patients with type I SBS were reviewed retrospectively from April 2013 to April 2019. Intestinal length was measured separately at the time of enterostomy and anastomosis, and the average growth (cm/month) in the proximal and distal intestinal lengths was calculated as the growth in intestinal length (cm)/the duration (month) from enterostomy to anastomosis. The hepatic function (total bile acids [TBA], alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase [ALP], γ-glutamyl transferase [GGT], total bilirubin [Tbi], and direct bilirubin [Dbi]) was assessed before anastomosis for 6 weeks and after anastomosis for 4 weeks to evaluate the changes in hepatic function from enterostomy to anastomosis.
Results: The average growth in the proximal intestinal length was 9.3 cm/month (±7.2) in neonates and 2.8 cm/month (1.3, 11.9) in infants and children, and the average growth in the distal intestinal length was 1.5 cm/month (0, 2.7) in neonates and 0.4 cm/month (0, 1.4) in infants and children.
There was an obvious increase in TBA, Tbi, Dbi, ALT, and AST before anastomosis and a visible decrease after anastomosis. The incidence of IFALD was 28.6% 1 month before anastomosis and 20.0% 1 month after anastomosis ($P < 0.05$).
Conclusion: In pediatric type I SBS with IFALD, restoration of intestinal continuity could alleviate liver injury. There was an intestinal compensatory effect on the growth in the intestinal length after resection. The better results in terms of the growth in intestinal length were seen in neonates among the pediatric type I SBS population.

关键字 intestinal continuity, short bowel syndrome, intestinal failure-associated liver disease, anastomosis, growth in intestinal length

分类：11. Gastroenterology Nutriology 消化与营养
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Effect of Secretory Immunoglobulin A on Necrotizing Enterocolitis in Neonatal Mice

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Our research aimed to establish C57BL/6J newborn mice modle of necrotizing enterocolitis(NEC) and investigate the protective effect of secretory immunoglobulin A (SIgA). Newborn C57BL/6 mice were divided into two group. NEC group: Mice were fed with artificial mouse food+hypoxia+lipopolysaccharide every day to induce NEC. SIgA intervention group: SIgA was added to mouse food while inducing NEC. Mice were killed on the fifth day. The survival rate of NEC group was 93.3% on third day, and it was 100% in SIgA intervention group. Activity of NEC group mice decreased; Mice in SIgA intervention group grew well. Finnally, the NEC model was successfully made. We preliminarily found that SIgA treatment can improve the survival rate and reduce the degree of intestinal injury of NEC neonatal mice.

关键字 necrotizing enterocolitis(NEC)；secretory immunoglobulin A (SIgA)；mice model

分类：11. Gastroenterology Nutriology 消化与营养
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Establishment of Megacystis Microcolon Intestinal Hypoperistalsis Syndrome model in mice by CRISPR-Cas9

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Background: Megacystis Microcolon Intestinal Hypoperistalsis Syndrome (MMIHS) is a rare congenital disorder. The main characteristics of this disease are abdominal distension, non-obstructive bladder dilation, small colon, poor peristalsis, and severe functional intestinal obstruction without structural atresia or stenosis. The disease is serious and has a high mortality rate. Due to the lack of effective treatment, patients generally have a poor prognosis. MMIHS is caused by heterozygous mutations of ACTG2 and homozygous mutations of MYH11, MYLK, MYL9 and LMOD1. Studies have shown that ACTG2 (γ-2 smooth muscle actin) is the most important pathogenic gene of MMIHS. Therefore, in this study, we used CRISPR-Cas9 (CRISPR-associated protein) genome editing of the murine ACTG2 gene to generate a heterozygous mutation, c.769C>T (p.R257C),and then verify whether the mutant can result in a similar MMIHS phenotype, so as to further study the pathogenic molecular mechanism of ACTG2 mutation on MMIHS.
Methods: gRNA (CAACGAGCGCTTCCGCTGCC) targeting ACTG2-R257C gene locus was designed and transcribed in vitro, and Donor vector was constructed at the same time. Cas9, gRNA and Donor vector are injected into the fertilized eggs of mice. Cas9 protein is combined to the target site under the guidance of gRNA to break the double strand of DNA, and then Donor Vector repair the broken double strand through homologous recombination to modify the target site of ACTG2 gene. After microinjection of fertilized eggs, embryo transfer, PCR and gene sequencing, homologous recombination positive F0 mice were obtained. F0 mice were mated with wild-type mice to obtain F1 mice. The positive F1 mice could be used for seed preservation and continued reproduction. Mutant mice and WT mice aged 6 to 12 weeks were selected to perform gastrointestinal motility analysis. Mice were administered a solution containing 6% carmine red dye and 0.5% methylcellulose in water via oral gavage (10 μl per gram of body weight) and then separately placed in clean cage and remove the padding. Food and water were available to the mice during the entire experiment. The total Gastrointestinal Transit transit was determined as the time required from gavage to the expulsion of the first red pellet.
Results: By using CRISPR-Cas9 (CRISPR-associated protein) genome editing technology, the mice successfully carried a ACTG2 heterozygous mutation. Intestinal dilation was observed in the mutant mice. Gastrointestinal motility analysis showed a significant increase in the total GI transit time of heterozygous mutant mice(380.3±134.1min for female and 504.7±143min for male) compared to WT mice(170.8±50.2min for female and 184.7±54.24min for male), both in female and male mice. Besides, there is a significant difference between mutant male mice and female mice, but no differences between control male and female mice.
Conclusion: We used CRISPR-Cas9 (CRISPR-associated protein) genome editing of ACTG2 to generate a MMIHS-Like mouse model presented with intestinal dilatation and the intestinal dysmotility, providing a suitable animal model for the subsequent study of the molecular mechanism of MMIHS induced by ACTG2 mutation.

关键字 CRISPR-Cas9，ACTG2，MMIHS

分类：11. Gastroenterology Nutriology 消化与营养
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Clinical analysis of etiology and risk factors in pediatric patients with acute pancreatitis and acute recurrent pancreatitis

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Objective To investigate the etiological characteristics of pediatric patients with acute pancreatitis (AP) and acute recurrent pancreatitis (ARP) and to evaluate the risk factors for ARP. **Methods** This retrospective study was performed to analyze the clinical data of children with AP. According to the presence or absence of recurrence, they were divided into AP group and ARP group to compare the etiological differences. According to etiology, they were divided into the biliary group, trauma group, drug group, metabolic group, and idiopathic group to compare the clinical features. For the measurement data with normal distribution, an independent sample T-test was used between two groups, and the one-way ANOVA was used among multiple groups. For the continuous variables without normal distribution, the Wilcoxon rank-sum test was used between two groups, and the Kruskal-Wallis test was used among multiple groups. The categorical variables were compared by using the χ^2 test. The Kaplan-Meier method and the log-rank test were used for the comparison of recurrence interval and recurrence rate. A Cox proportional hazards model was used to analyze the risk of ARP. **Results** A total of 188 children with AP were included in this study, and 33 children were diagnosed with ARP. The recurrence rate was 17.6%. The common etiology of AP were biliary(38.7%) and idiopathic(36.1%),while ARP was idiopathic(56.7%)) which were statistically significant (χ^2=15.141, P=0.004).The incidence of female and pre-school age (2~6 years old) in the biliary group was significantly higher than the drug group, metabolic group, and idiopathic group, while the incidence of school-age (6 ~13 years old) was significantly lower than three groups above. Children in the drug group had the longest length of hospital stay and the lowest level of white blood cell count and neutrophils. The proportion of severe AP was significantly higher than the idiopathic group. The interval between recurrence in children with ARP caused by mild AP and moderate-severe AP or idiopathic factors was statistically longer than that in children with severe AP or causes known. Multivariate Cox regression analysis showed that the severity of AP was a risk factor for children with ARP(P=0.036 95%Cl:0.059~0.906). **Conclusions** The common etiology of children with AP was biliary, especially in preschool children while the children caused by drugs had a higher incidence of severe AP and longer length of hospital stay. The common etiology of children with ARP was idiopathic and genetic mutation testing should be performed for further diagnosis. Additionally, the severity of AP was the risk factor of ARP.

关键字 Acute pancreatitis; Acute recurrent pancreatitis; Etiology; Children;

分类：11. Gastroenterology Nutriology 消化与营养
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Appropriately sequential application of intravenous lipids in pediatric patients with intestinal failure

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Background: Although many studies focused on the effect of Omegaven lipid on liver function in pediatric patients with intestinal failure (IF), the studies of how to select fat emulsion following improved liver function with Omegaven application were still less. Thus, the aim of this study was to assess appropriately sequential application of intravenous lipids and its effect on liver function in children with IF.
Methods: We recruited 25 children with IF on sequential application of lipids, which began with Omegaven and weaned with 20% lipids (50% medium-chain triglycerides and 50% long-chain triglycerides (MCT/LCT) lipid or SMOF (30% soybean oil, 30% medium-chain triglycerides, 25% olive oil, and 15% fish oil) lipid) from January 2014 to June 2020. When children had liver damage (the levels of any three of liver indicators, including total bile acids (TBA), alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (AKP), gamma glutamyl transferase (γ-GT), total bilirubin (TB), or direct bilirubin (DB) were two times higher than normal value), Omegaven was used in parental nutrition, if the liver function improved, we switched to 20% lipids. Liver function were measured once a week.
Results: With Omegaven therapy, the value of TBA, ALT, AST, and TB decreased significantly, the value of DB and γ-GT decreased. However, AKP increased, but no statistical significance. The weight gain was higher increased during using 20% lipids than during using Omegaven. After application of MCT/LCT lipid, the level of TBA, ALT, AST, AKP, γ-GT, and TB increased. The level of DB decreased. However, after application of SMOF lipid, the level of AKP, γ-GT, TB and DB decreased. But the level of TBA, ALT, and AST increased.
Conclusion: SMOF lipid delays liver injury following improved liver dysfunction with Omegaven lipid in children with IF.

关键字 lipid PNALD

分类：11. Gastroenterology Nutriology 消化与营养
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Blue rubber bleb nevus syndrome: A single-center case series in twelve years

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Objectives: To present and analyze the clinical characteristics of pediatric patients with blue rubber bleb nevus syndrome and to improve understanding in order to give an earlier diagnosis and timely treatment.
Methods: A retrospective single center study was conducted on 8 patients with blue rubber bleb nevus syndrome from 2009 to 2021. Data were analyzed including clinical feature, diagnostic workup and results, gene detection, treatment and follow-up.
Results: 5 children (62.5%) developed the disease in infancy, which initial symptom were all cutaneous vascular malformations. All children had chronic refractory anemia and gastrointestinal bleeding. Cutaneous lesions were observed in 87.5%, 1 child had multiorgan involvement. Gastrointestinal vascular malformations were observed in 100%, lesions were more common in small intestine than in stomach or colon. No somatic mutation in TEK was found in our children. Diagnostic interval was on average 4.7 years. 87.5% children received at least one endoscopic or surgical intervention, however, none of these methods can effectively cure and prevent recurrence of lesions. 2 children treated with sirolimus for more than 8 years, only 1 have satisfactory therapeutic effect. Besides,1 child has growth retardation and emotional problems during follow-up.
Conclusions: Blue rubber bleb nevus syndrome needs to be considered when find bluish nodular cutaneous lesions, chronic anemia or gastrointestinal bleeding of unknown origin. Sirolimus does not apply to all patients, further studies are required to evaluate its long-term safety and the final effective valley concentration for children.

关键字 Blue rubber bleb nevus syndrome，vascular malformations，anemia，sirolimus

Category: 11. Gastroenterology Nutriology 消化与营养
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Role of Probiotics in Modulating Gastrointestinal Inflammation among Chronic Cholestatic Children: A Pilot Study

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Abstract Content Chronic cholestasis is closely related to small intestinal bacteria overgrowth, often manifested as prolonged diarrhea. Probiotics have been shown to reduce frequency and duration of diarrhea, as well as having anti-inflammatory effect by affecting gut microbiota. However, its role on pediatrics with chronic cholestasis has never been studied. Objectives: A pilot study to investigate the role of probiotics in improving gastrointestinal inflammation among chronic cholestasis children in Cipto Mangunkusumo Hospital, Indonesia.

Methods This is a randomized, double-blinded, single centered trial among children with chronic cholestasis (cholestasis occurred > 4 weeks, as evidenced by laboratory findings with no history of antibiotics usage one month prior) at tertiary hospital in Indonesia between October 2020 and August 2021. A total of 31 subjects were randomly allocated into intervention group (15 subjects) and control group (16 subjects) using randomization table. Each subject completed a twice-daily regimen of probiotics or placebo for 28 days according to initial allocation. The primary outcomes were fecal calprotectin level and the secondary outcomes were liver function tests and fecal leukocyte count.

Results After 28-days of intervention, there was no statistically significant difference between the post-experiment faecal calprotectin between the intervention group compared to control group (126.1 (44 — 220) vs 86.1 (28.2 — 159.3), p=0.33). Pre- and post-intervention liver function tests including ALT, AST, ALP, GGT, bilirubin, and albumin were also not significantly different in both groups. There were also no significant decrease of fecal leukocyte count on post-experiment measurement in the intervention group compared to control group (p=0.46). Three subjects complained about bloating or acute diarrhea upon consumption, but no medications were necessary.

Conclusion Four weeks course of probiotics supplementation in chronic cholestatic children did not significantly lower gastrointestinal inflammatory marker fecal calprotectin, and did not improve liver function markers and reduce fecal leukocyte count significantly. Longer duration, mixture of prebiotics and probiotics, and dosage alteration of intervention should be considered for further investigations.

Key words chronic cholestasis; probiotics; fecal calprotectin; liver function tests
Reference None

分类：11. Gastroenterology Nutriology 消化与营养
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Predictive factors for Catheter-Related Bloodstream Infections in Children with Intestinal Failure

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Background: Children with intestinal failure (IF) have frequent catheter-related bloodstream infections (CRBSIs). This study aimed to analyze the clinical presentation of CRBSIs in children and to detect possible predictive factors for CRBSIs in children with IF.

Methods: This six-year retrospective study was conducted among IF children with CRBSIs at a territory medical center. Clinical data were collected, including data of temperature and gastrointestinal symptoms. Blood/catheter culture, fecal tests, and calculation of inflammatory index were performed, which were obtained within one week since CRBSI onset.

Results: Fifty children with 87 CRBSIs were identified, of which there were 17 suspected and 70 confirmed cases. Seventy-two pathogens were cultured from 70 positive blood cultures: 66.7% were gram-positive organisms, 22.2% were gram-negative organisms, and 11.1% were fungal organisms. Overall, 48.6% were enteric organisms; 47.2% of bacterial pathogens were consistent between fecal and blood cultures. Moreover, 46.3% fecal routines showed abnormalities including increased white blood cells, occult blood positive and presence of fat droplets. The consistent symptom at onset of CRBSIs was fever and gastrointestinal symptoms including increased stool output, abdominal distension, or both. C-reactive protein (CRP) and procalcitonin (PCT) were elevated, i.e., 16 mg/L (interquartile range [IQR] 8.0-43) and 0.48 ng/mL (IQR 0.2-1.76), respectively.

Conclusion: IF children had a high rate of CRBSIs, of which larger proportions were due to gram-positive and enteric organisms. Fecal routines and bacterium culture should be regularly examined. Fever and/or gastrointestinal symptoms, combined with elevated CRP and PCT, is conducive to the early diagnosis of CRBSIs in IF patients.

关键字 enteric pathogens, gastrointestinal symptoms, fecal examination

分类：11. Gastroenterology Nutriology 消化与营养
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Therapeutic effect of celecoxib on experimental corrosive esophageal injury

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Background:Corrosive esophageal injury is still a common health problem in developing countries. It has been reported that 75%-80% of patients are child under 5 years old, which are caused by misuse; secondly, they are mainly concentrated in adolescents and youth, and most of them are caused by suicide. Researches showed that alkaline etchants are more common than acid etchants in corrosive esophageal injury. Patients ingesting strong alkali corrosives have varying degrees of esophageal damage, such as acute necrosis of the esophagus, bleeding, ulcers and perforation, etc. The probability of severe corrosive esophageal injury leading to stenosis can be as high as 70~100% which would affect children's whole life. To date, there are no effective drugs for corrosive esophagitis. Celecoxib can selectively inhibit COX-2 to exert anti-inflammatory effects. This study was designed to evaluate the therapeutic effect of celecoxib on the rat experimental model of corrosive esophageal injury by NaOH.Methods:Thirty-six male Wistar rats weighing about 200g were randomly divided into three groups, namely sham operation group (S group), model group (M group) and treatment group(T group). In this experiment, Gehanno's surgical method was used. In short, 1 ml of 30% NaOH was injected into the esophagus area through a gastric puncture after opening the abdomen, and it was left for 1 minute to corrode the esophagus and cause damage. Then, abdomen was lavaged with saline and closed. The S group did not undergo surgical treatment after laparotomy. Both the M group and the T group were given 30% NaOH. After the operation, the treatment group was intragastric with celecoxib 20mg/kg per day. All rats were sacrificed on 28 days after surgery for test. Esophageal tissues were obtained for H&E staining, Toluidine Blue staining and immunohistochemistry.Results:Compared with the S group, the weight of rats in the M and T groups decreased significantly at 28 days after the operation. Compared with the M group, the weight of the rats increased significantly with the treatment of celecoxib，P=0.003. At the same time, there were almost no adhesions in the abdominal cavity in the S group, but the adhesion scores in the M and T groups were significantly higher than those in the S group (P<0.05). Besides, the adhesion scores in the M group were significantly higher than those in the T group (1.6±0.9 vs.3.0±1.3, P =0.016). Compared with the control group, more submucosal collagen of the esophagus，damaged muscularis mucosa and muscularis propria collagen deposition were found by esophageal slices in the M group. In the T group, tissue damage of esophagus were alleviated with the treatment of celecoxib. Compared with the S group (44.50±0.57), the number of mast cells in the esophagus of rats in the M roup(117.00±59.17) increased significantly, P=0.019; after the treatment of celecoxib, the number of mast cells in the T group was significantly reduced (36.50±0.58,P=0.019).Conclusion：The ultimate goal of treating corrosive esophageal injury is to control the inflammatory response at the injured site and further damage to the tissue, to reduce collagen deposition, and ultimately reduce the formation of extensive scars and prevent stenosis. There have been many drug experiments to prevent the formation of esophageal stricture through anti-nflammatory and anti-fibrosis. In this experiment, cyclooxygenase-2 (COX-2) inhibitor celecoxib was used to prevent and treat corrosive esophageal injury. The results showed that, compared

with the chronic injury group, celecoxib significantly reduced the adhesion of the abdominal cavity and surrounding tissues of the esophagus, significantly improved the appearance of the rat esophageal serous membrane, significantly reduced the damage of the esophageal tissue, and reduced the inflammatory response of the esophageal tissue.

关键字 Corrosive esophageal injury, selectively COX-2 inhibitor, inflammation

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The role of short-chain fatty acids in the gut microbial-gut-brain axis

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Objective: Short-chain fatty acids are mainly produced by dietary fiber metabolism through gut microbiota.Short-chain fatty acids are one of the factors involved in gut microbial - gut-brain axis interactions.
Methods: This review is discussed about the role of short-chain fatty acids in the gut microbial - gut-brain axis.
Results: This paper describes the effects of short-chain fatty acids on the cellular system and their interactions with gut-brain signaling pathways, including the immune, endocrine, neural, and humoral pathways.
Conclusion: The mechanism of the short chain fatty acids in the gut microbial-gut-brain axis still needs further investigation, the mechanism of the short chain fatty acids in regulating neuroimmunoendocrine function will provide new therapeutic ideas for the central nervous system diseases.

关键字 short-chain fatty acids，gut microbiota，gut-brain axis

分类：11. Gastroenterology Nutriology 消化与营养
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Clinical analysis of 6 cases with pegaspargase-associated pancreatic pseudocyst in children

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【Abstract】Objective To investigate the clinical characteristics and treatment of pegaspargase-associated pancreatic pseudocyst in children. Methods The clinical data of 6 children with pegaspargase-associated pancreatic pseudocyst were analyzed retrospectively, and the clinical characteristics and treatment of pegaspargase-associated pancreatic pseudocyst were analyzed. Results (1) Among the 6 children, there were 4 males and 2 females, with a median age of 9.5 years(5years-13years). The total number of doses of pegaspargase was 2, the median time from the last application of pegaspargase chemotherapy to the onset of pancreatitis was 11.0 days (9 days-18 days), and abdominal pain was the most important manifestation of pancreatitis. The median time from the onset of pancreatitis to the diagnosis of pancreatic pseudocyst was 42.5 days (32days-152 days). None of the 6 children with pancreatic pseudocyst had clinical symptoms when pancreatic pseudocyst was diagnosed, and all of them were treated conservatively first, with 1 case developing intermittent abdominal distension or nausea after eating. (2) All of the 6 cases of pancreatic pseudocyst enlargement reported during conservative treatment. (3) All of the 6 cases underwent endoscopic treatment later, 3 cases of which were treated with endoscopic ultrasound-guided transgastric drainage, and 3 cases received ERCP-guided transpapillary drainage. (4) One child had postoperative complications of acute pancreatitis, which were improved after symptomatic treatment. One child who underwent ERCP-guided transpapillary drainage was converted to surgical treatment due to pancreatic duct stenosis, and pancreatic pseudocysts of the remaining five children resolved 10 days - 4 months after surgery. Conclusions The incidence of pancreatic pseudocyst is increased in the treatment of acute lymphoblastic leukemia with pegaspargase chemotherapy. During conservative treatment, when the pseudocyst progressively enlarges or shows clinical symptoms, endoscopic drainage should be the first-choice treatment, and surgery should be used for failures of endoscopic drainage treatment.

关键字 Pegaspargase; Pancreatic pseudocyst; Children

分类：11. Gastroenterology Nutriology 消化与营养
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Early recognition and diagnosis of Henoch-Schonlein purpura in children with abdominal symptoms

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Background: Henoch-schonlein purpura (HSP) is an inflammatory disease in which immune complexes formed under the body’s immune-mediated deposition are deposited in small blood vessels throughout the body. Mainly affected. HSP is clinically manifested as non-thrombocytopenic purpura, often located in the lower limbs and buttocks, and can be accompanied by gastrointestinal, joint, and kidney involvement. It is mostly benign and self-limiting. The prognosis is good. It usually resolves within 6 to 8 weeks, but some are affected. Children can have recurrent attacks. 50%～80% of HSP affects the gastrointestinal tract. Diffuse intestinal colic is caused by submucosal or subserosal hemorrhage and edema. Abdominal HSP is easy to be misdiagnosed, missed and delayed before a typical rash appears. , And serious complications, such as intussusception, massive gastrointestinal bleeding, intestinal perforation, etc., and even unnecessary appendicitis surgery. The etiology of HSP is still unclear, and a variety of pathogenic microorganisms may be the predisposing factors of HSP.
Methods: Analyzing the condition, endoscopic manifestations, and pathological characteristics of abdominal HSP to identify and diagnose early is an important method to block the progression of the disease and avoid serious complications.
Results: The main manifestation of abdominal HSP was gastrointestinal symptoms. Children with abdominal symptoms as the first manifestation were easily misdiagnosed when they did not have typical skin purpura. In terms of clinical symptoms, abdominal pain is the most common and prominent, which can be mild or severe, most of which are severe abdominal pain. The location is mainly around the umbilical cord and the upper abdomen, which may be accompanied by vomiting, hematemesis, diarrhea, blood in the stool, and abdominal distension; intussusception , Intestinal perforation, intestinal obstruction and shock can occur in a very small number of children. Abdominal pain is caused by aseptic inflammatory changes in the small arteries and capillary walls of the gastrointestinal tract, which increase the permeability and fragility of the blood vessel wall, and cause serous exudation around the blood vessels, which makes the intestinal ischemia and hypoxia, and dysfunction Caused by.In recent years, with the rapid development of children's endoscopy technology, endoscopy has become more and more widely used in children with abdominal HSP, including gastroscopy, colonoscopy, capsule endoscopy, and enteroscopy. Vasculitis of HSP can involve the esophagus, gastric fundus, gastric body, gastric horn, gastric antrum, duodenal bulb and descending part. The degree of mucosal damage ranges from local congestion and edema, spot or focal erosion, stripe erosion, and mucosa Bleeding, hematoma-like bulge and multiple ulcers vary. The most severe and severe damage is the descending part of the duodenum, followed by the bulb, antrum, fundus, and body of the stomach. The esophagus and gastric angle are rarely involved. And to a lesser degree. The histopathological characteristics of children with abdominal HSP are inflammatory changes in capillaries, focal necrosis of the vessel wall, necrotizing enteroarteritis, and a large number of lymphocytes and eosinophils infiltrated in the mucosa, and ulcers can be seen.
Conclusion: Abdominal HSP has gastrointestinal symptoms before the onset of purpuric rash, and it has various forms. Children with acute abdomen should be highly vigilant against abdominal HSP. If possible, gastroscopy can be performed as soon as possible

to assist in diagnosis. Avoid misdiagnosis, missed diagnosis, and delayed diagnosis. The characteristic mucosal changes under gastroscopy can assist in the early diagnosis of abdominal HSP, but the indications of endoscopy should be strictly controlled to avoid increasing the pain of the child and the burden on the family.

关键字 child; Henoch-Schonlein purpura; gastroscopy

分类：11. Gastroenterology Nutriology 消化与营养
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Pediatric Meckel's Diverticulum: Report of 32 Cases

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Background: Meckel's diverticulum is the most prevalent congenital anomaly of the gastrointestinal tract, resulting from incomplete obliteration of the omphalomesenteric duct in the developing embryo. It is the true diverticulum of the small intestine often located 2 feet proximal to the ileocecal valve and could be found in almost any age group. The walls of the Meckel’s are lined by the intestinal mucosa, also frequently contain ectopic tissue. Gastric tissue is the most common, and next is pancreatic tissue, rarer forms include ectopic duodenal and colonic tissue. Ectopic tissue regularly makes the Meckel’s symptomatic. It may remain completely asymptomatic, or it may present with severe complications such as obstruction, GI-hemorrhage, and inflammation, Obstruction and GI-hemorrhage are both common presentations in pediatric patients. For pediatric patient with symptomatic Meckel’s may be quite alarming and anxiety-provoking for their parents. The common symptoms are fever, vomiting, abdominal pain, and bloody stools, which may be caused by acid secretion from the ectopic gastric mucosa within the diverticulum and mimic such disorders as Crohn's disease, appendicitis and peptic ulcer disease. Although Meckel's diverticulum is common, it is often difficult to diagnose because of lacking of typical symptoms. Technetium (Tc) 99m pertechnetate radionuclide scanning may visualize the Meckel’s by tracing accumulates in certain tissues like functional ectopic gastric tissue. But the result is influenced by several factors, such as bleeding and premedication with certain drugs. Besides, Meckel’s can be diagnosed by using imaging modalities like ultrasound. One of the aims of this report is to highlight the different diagnostic modalities of Meckel's diverticulum which could greatly facilitate the diagnosis of pediatric Meckel's diverticula.
Method: We report a review of 32 cases of suspected and 16 in 32 cases of surgical Meckel's diverticulum among pediatric patients from one single institution from 01 January 2020 to 31 April 2021. Data were collected including diagnosis, sex, age, pathology and outcome.
Results: Of the 32 suspected cases, the male to female gender ratio is 29:3. 12 of 32 cases present positive for Technetium (Tc) 99m pertechnetate radionuclide scanning. 11of 32 cases present positive for ultrasonography. 16 of 32 cases has abdominal surgery. 1 of 16 cases involves a male patient appearing with a positive result of ultrasonography, instead surgery revealed no diverticulum arising from the ileum. The rest of the 16 cases diagnose Meckel’s, 6 of them contained gastric heterotopic tissue. The male to female gender ratio is 14:1 of the Meckel’s cases. More than half of all children with Meckel’s who required surgery were <5 years. 9 of 16 cases present positive for Technetium (Tc) 99m pertechnetate radionuclide scanning. 9 of 16 cases present positive for ultrasonography. 3 of 16 cases present positive both of Technetium (Tc) 99m pertechnetate radionuclide scanning and ultrasonography. 14 of 16 cases present positive for Technetium (Tc) 99m pertechnetate radionuclide scanning or ultrasonography. 7 of 16 cases present negative for Technetium (Tc) 99m pertechnetate radionuclide scanning but positive for ultrasonography. 1 of 16 cases present positive for capsule endoscopy. Significantly, a male patient with twice negative result of Technetium (Tc) 99m pertechnetate radionuclide scanning, show a positive result for ultrasonography and diagnose with Meckel's diverticulum by surgery.

Conclusions: As stated above, symptomatic Meckel’s can present kinds of atypical symptom, which makes it difficult to confirm the diagnosis. For pediatric patients, faster and more accurate to diagnosis is necessary, especially using noninvasive method of achieving diagnosis. Thus, the cooperation of Technetium (Tc) 99m pertechnetate radionuclide scanning and ultrasonography can increase rates of diagnosis.

关键字 儿童， 麦可尔憩室

分类：11. Gastroenterology Nutriology 消化与营养
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Fecal microbiota transplantation alleviates symptoms in FGIDs children with predominant abdominal bloating via modulation of the gut microbiota and metabolome

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Objectives: Functional gastrointestinal disorders (FGIDs) are disorders of gut-brain interaction without any underlying structural abnormalities. Fecal Microbiota Transplantation (FMT) has been reported to induces significant relief in adults with FGIDs. In this study, we aim to evaluate its effect on treating FGIDs children with bloating, and explore fecal microbiota changes and metabolic activities during FMT treatment.
Methods: We followed 12 patients with FGIDs who underwent FMT for the treatment of bloating, defined by the ROME 4 criteria. Clinical data, including demographics, clinical features, and laboratory indexes were assessed. Stool samples were collected at baseline, 1, 2, 4 and 8 weeks for 16S rRNA gene sequencing and targeted metabolomics analysis.
Results: Abdominal bloating was improved in all patients (12/12, 100%) by FMT either via nasointestinal tube (5/12, 41.67%) or oral capsules (7/12, 58.33%). Meanwhile, FMT significantly improved the symptoms of abdominal pain (patients number before FMT, 7; number after FMT, 2; P=0.039), diarrhea (patients number before FMT, 5; number after FMT, 1; P=0.028), and in Bristol stool scores (P=0.026) after 8 weeks of intervention. Baseline Shannon index indicated that microbiota showed lower diversity in FGIDs patients compared to those of healthy controls and donors. Patients receiving FMT had an increase in diversity and abundances of fecal microbiota, which shifted closer to the donors and healthy control group. Moreover, these enrichment effects of FMT were also found in the increased concentrations of fecal short-chain fatty acids (SCFAs), including 4-methylhexanoic acid, indole-3-propionic acid and butyric acid.
Conclusions: Our results indicate that FMT is a useful and safe tool for the treatments of abdominal bloating children. FMT changed some gut bacteria and metabolites in abdominal bloating patients toward a healthy state.

关键字 children; fecal microbiota transplantation; abdominal bloating; gut microbiota; metabolome

分类：11. Gastroenterology Nutriology 消化与营养
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Effects and concurrent actions of Bifidobacterium longum CECT7894 and IFX on DSS-induced colitis mice models

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Objectives: To investigate the effect of Bifidobacterium longum CECT7894 and infliximab in DSS-induced colitis mice models and concurrent actions of these two treatment methods.
Methods: Treat 6-8-week-old C57BL/6 mice with probiotics (Bifidobacterium longum CECT7894) prospectively for 5 consecutive days. Subjects are processed by DSS to induce colitis, followed by various managements using different combinations among probiotics, and infliximab to simulate treatment options in the circumstances of colitis. In 1 week, scarify the mice for further analysis, including weighing of the mice, measuring of colon length, histopathological examination using colon mucosal damage index (CMDI), and flow cytometry for CD25+ Foxp3+ expression.
Results: Firstly, IFX and Bifidobacterium longum can relieve the weight loss of mice models. But when they are jointly administered, the condition is not as good. It’s in accordance with the impact on length of colon. Secondly, in the CMDI assessment, IFX and Bifidobacterium longum can relieve the index. Co-use does not generate stronger curing efficacy. Finally, IFX showed effectiveness in the flow cytometry test, while probiotics has almost no impact on the percentage of CD25+ Foxp3+ expression levels of Treg cells.
Conclusions: Bifidobacterium longum and IFX can attenuate the impact of colitis on weight loss, colon length shortening and CDMI in DSS-induced colitis models. IFX plays an important role in Treg expression regulation. Co-utilization of these two treatment options is not necessary.

关键字 Bifidobacterium longum; IFX; colitis; Treg

分类：11. Gastroenterology Nutriology 消化与营养
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Dynamic Changes of Fecal Microbiota and Bile Acid Metabolism in Pediatric Crohn’s Disease During Exclusive Enteral Nutrition Treatment

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Background: Gut microbiota dysbiosis and bile acid (BA) metabolism alteration is closely associated with Crohn’s disease (CD). Exclusive enteral nutrition (EEN) is widely used to treat pediatric CD; however, the community structure and function of gut bacterial and fecal BA during EEN treatment in Chinese children with CD remains obscure. This study aimed to investigate the dynamic changes of the fecal microbial community and BA metabolism in pediatric CD patients during EEN therapy.
Methods: We performed a metagenomic shotgun sequencing to determine the compositions of microbial communities in a pediatric CD cohort undergoing EEN therapy to induce disease remission. And assessed their association with the fecal levels of primary and secondary BAs.
Results: We found characteristics of fecal BA composition in paediatric CD patients before EEN treatment were represented by lower unconjugated BAs and secondary BAs, including 3-epideoxycholic acid, deoxycholic acid, β-hyodeoxycholic acid, lithocholic acid, isolithocholic acid and taurodeoxycholic acid. EEN treatment increased unconjugated secondary BAs and shifted its composition as well as its functional capabilities in the pediatric CD patients toward a healthy status. The variable importance in projection (VIP) score for BA showed that hyocholic acid (HCA) contributed significantly to CD patients’s clinical remission. However, whole-genome shotgun sequencing showed no significant difference in bacterial alpha and beta diversity between individuals with CD before and after EEN treatment.
Conclusion: Fecal BAs are associated with Crohn’s disease (CD) development and response to EEN therapy. The characteristic of children with CD is correlated with low concentration of unconjugated BAs and secondary BAs in the gut. EEN diminished the CD-associated BAs dysbiosis but was deficient in increasing HCA.

关键字 Crohn's disease; gut microbiota; bile acids; exclusive enteral nutrition

分类：11. Gastroenterology Nutriology 消化与营养
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Efficacy and safety of percutaneous endoscopic gastro-jejunostomy (PEG-J) for patients with pediatric chronic intestinal pseudo-obstruction (PIPO)

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BACKGROUNDS: Pediatric chronic intestinal pseudo-obstruction (PIPO) is an intractable rare digestive disease manifesting persistent small bowel distension without any mechanical cause. Intestinal decompression and appropriate nutritional support are the keys of treatment, but conventional method including nasogastric/nasoduodenal/nasojejunal tubes are invasive and painful. And the patients usually need two or more tubes simultaneous. Therefore, a less invasive and tolerable method which has both decompression and nutrition treatments is urgently desired. We conducted a pilot study and assessed the efficacy and safety of percutaneous endoscopic gastro-jejunostomy (PEG-J) as decompression and nutrition therapy in PIPO patients.
METHODS: Five definitive PIPO patients (3 males and 2 females) were enrolled. All patients received PEG -J decompression therapy. The age of onset was within 1 year old of 4 cases, and over 1 year old in 1 case. 4 cases were clearly identified as ACTG2 gene mutations, and 1 case had no obvious gene mutations. Catheterization time, nutritional intake, percentage of intravenous nutrition, serum albumin level, complications related to catheterization were recorded.
RESULTS:
1. The catheterization time of children with PIPO is significantly prolonged. The PEG-J catheterization time of non-PIPO children is generally about 1 hour. In this study, the first PEG-J catheterization time of the 5 cases of PIPO children was 3 hours on average. The dilatation of the stomach and duodenum leads to changes in the anatomical position, which is related to the difficulty of inserting the J tube.
2. The 5 patients were fasted for 7-20 days and gastrointestinal decompression due to gastric dilatation before the catheterization. After the catheterization, 3 children achieved total enteral nutrition in 10-30 days, and 2 children reached 80 % enteral feeding.
3. There was no significant decrease in serum albumin levels.
4. The main complications related to catheterization include: 1) 1 case of diarrhea: related to the depth of the catheter; 2) 2 cases of jejunal catheterization: related to gastrointestinal decompression, one case of multiple slips and reinsertion of the catheter; 3) 1 case of subcutaneous emphysema. There was no catheter-related gastrointestinal infection, gastrointestinal perforation, bleeding and other acute complications.
5. Survival status: All 5 cases of patients survived, 4 cases are still in catheterization, and the catheterization time is 4 months to 2 years.
CONCLUSION: PEG-J tube can basically meet the needs of enteral nutrition and gastrointestinal decompression in patients with PIPO, but when the patient’s gastric retention increases and the stomach dilates, the jejunal tube is prone to slip off. Therefore, the PEG-J tube for such patients Postoperative management still needs further research. In addition, gastrointestinal motility problems and gastric dilatation problems in PIPO patients lead to a significant increase in the initial PEG-J catheterization time.

关键字 PIPO, PEG-j

分类：11. Gastroenterology Nutriology 消化与营养
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The relationship of gastric microbiota and Helicobacter pylori infection in pediatrics population

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Objective: To explore the relationship between helicobacter pylori infection and gastric flora in children from the perspective of microecology.Methods: Stomach mucosa samples from children who underwent gastroscopy from September 2018 to May 2019 were collected and divided into Hp-positive group (group A), Hp-negative group (group B), and post-treatment group (group C)). Sequencing and analysis of gastric mucosa specimens were performed by 16SrDNA high_x0002_throughput sequencing technology and microbial functions were predicted using the software PICRUSt. Results: Endoscopic gastric mucosal biopsy specimens from 55 children with gastrointestinal symptoms were collected, 37 of them were H pylori positive (23 non_x0002_peptic ulcer and 14 peptic ulcer) and 18 were H pylori negative. In addition, 11 specimens were collected from H pylori positive children who performed second endoscopy in four weeks after therapy. The gastric microbiota of H pylori positive children were mainly dominated by Helicobacter in genus (95.43%). The microbiota richness and diversity of H pylori positive children were lower than that of H pylorinegative children. The richness and compositions after therapy were closer to the characteristics of H pylori negative children. For predicted functions, higher abundance in pathways of infection diseases, cancer and lower abundance in the pathways of amino acid, lipid and carbohydrate metabolism were found in H pylori positive group than H pylori negative group.Conclusion: The characteristics of gastric microbiota were affected by H pyloriinfection and the richness and diversity of gastric species were inverse correlation with H pylori infection in children. Eradication therapy was helpful to restore shifted gastric microbiota

关键字 children, Helicobacter pylori, gastric microbiota

分类：11. Gastroenterology Nutriology 消化与营养
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Etiology and clinical characteristics of infantile cholestatic hepatopathy in hospitalized children of single center in Hebei

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Objective
The purpose of this study is to analyze the etiology and clinical characteristics of infantile cholestatic hepatopathy hospitalized Children in Hebei.
Materials and Methods
A retrospective, descriptive study was undertaken of 168 children 0-18 years admitted to Hebei Children's Hospital for ICH from January 2018 to December 2020. Clinical data including gender, age, hospitalization time, etiology and other data were collected. the etiology and clinical characteristics of infantile cholestatic hepatopathy hospitalized Children were analyzed.
Results
The records of 168 cases were reviewed for this study. The etiology and clinical characteristics of infantile cholestatic hepatopathy hospitalized Children as follows: (1) Among 168 hospitalized children with infantile cholestatic hepatopathy, there were 105 males and 63 females, with a male to female ratio of 1.7:1. (2) The children ranged in age from 6 hours to 1 year, with a median age of 0.16 years. Among them, 2 cases were neonates, and the rest were infants over 28 days old.(3) There were 65 cases admitted in 2018, 53 cases in 2019 and 50 cases in 2020.(4) Shijiazhuang (55 cases), Xingtai (43 cases) and Handan (32 cases) were the top three sources of these patients, accounting for about 77% of all the patients. (5) The average length of hospitalization of 168 children was 14.3 days. 74 patients were hospitalized for less than 10 days, 62 patients for 10-20 days, 23 patients for 20-30 days, and 9 patients for more than 30 days.(6) The hospitalization cost was between 2663.98 yuan and 84580.07 yuan, with an average hospitalization cost of 11969.27 yuan. 147 cases, accounting for 87.5% of all patients, cost between 5000 yuan and 20000 yuan.(7) Of the 168 cases, 18 cases had a history of asphyxia, 37 cases had premature birth.(8) Among them, there were 21 cases of infectious diseases, 17 cases of genetic metabolic diseases, 4 cases of structural abnormalities of the biliary tract, 1 cases of total parenteral nutrition associated cholestasis, 2 cases of Congenital hypothyroidism, and 123 cases of unknown etiology. Among infectious diseases, the highest incidence was cytomegalovirus infection, with a total of 14 cases. Among the 17 cases of genetic metabolic diseases, 6 cases were caused by Citrin deficiency. Other etiology included progressive familial cholestasis in the liver in 4 case, A Dubin-Johnson syndrome in 3 cases, Niemann-Pick disease in 2 cases, congenital carnitine deficiency in 1 cases, and erythropoietic protoporphria in 1 cases. All the 4 cases of biliary atresia were diagnosed by cholangiography. (9) All the 168 cases were treated with yellow staining of skin and sclera, including 9 cases with anorexia, 17 cases with vomiting, 11 cases with diarrhea, 78 cases with darker urine color, 51 cases with lighter stool color, 15 cases with enlarged liver and 20 cases with enlarged spleen, and all the children had no symptoms of irritability.(10) All the children underwent abdominal ultrasound examination, and the hepatobiliary system was abnormal to varying degrees. In all the 4 children with biliary atrexia, the abdominal MRI examination indicated that the gallbladder was not filled or poor filling, and the extrahepatic bile duct was not displayed or unclear.

Conclusions
ICH is more common in males and usually occurs at a younger age, with no difference in incidence among years. ICH children hospitalized for a long time, cost a lot, bring a great economic burden to the family and society. In the infectious factor group, cytomegalovirus infection was the main factor. Citrin deficiency was the main factor in the genetic and metabolic factor group. Diseases of the biliary tract system were mainly congenital biliary atresia. Abdominal MRI is useful in the diagnosis of biliary atresia. The etiology and pathogenesis of ICH were complex, and the clinical features of ICH due to different etiologies lack specificity, so its diagnosis and treatment were very difficult.

关键字 Cholestatic hepatopathy ； Infant ； Etiology ； Clinical features

Nephrology

肾脏

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The pathological types in infants with renal diseases in a single center

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Background: Data regarding renal pathology in infants (< age 3yr) were limited. The aim of this study was to analyze the causes of renal disease and their clinical presentations in infants patients who underwent renal biopsy.

Method: A retrospective analysis was made on 117 cases who were performed renal biopsy under 3 years old in the Department of Nephrology and Rheumatology, Shanghai Children's Hospital from January 2009 to December 2020. The clinical data were collected and children who were suspected with hereditary diseases were examined for gene.
Results: (1) The proportion of 117 renal biopsy infants in all renal biopsy patients was 6.5% (117/1796). Compared with 2009-2014, the ratio of renal biopsy at 0-3 years in 2015-2020 was increased (P<0.05). (2) The indications for biopsy were nephrotic syndrome (NS) in 55.6%(steroid-dependent NS in 52.3%, steroid-resistant NS in 40%, 1 case was NS with Hepatitis B virus infection), microscopic hematuria (with / not with proteinuria) in 29.9%, gross hematuria in 8.5% (9 cases of Alport's syndrome and 1 case of membranous nephropathy), isolated proteinuria in 5.1%. Minimal change disease was the most frequent diagnosis (27.4%), followed by Alport's syndrome (22.2%), glomerular minor lesion (12%), focal segmental glomerulosclerosis (FSGS, 10.3%), IgM nephropathy (7.7%), mesenchymal proliferative glomerulonephritis (7.7%) and so on. 24 infants (20%) were found disease-related genetic variations. (3) Compared with infants aged 2-3ys, the renal biopsy infants aged 0-2ys had higher detection rate of FSGS (P<0.05).
Conclusions: The proportion of renal biopsy in infants had increased significantly in the past five years. In clinic, attention should be paid to gross hematuria in infants, which may be related to hereditary renal disease. The combination of renal biopsy and gene examination could more accurately identify the causes of disease.

关键字 Renal biopsy; infants; kidney disease; gene

分类：17. Nephrology 肾脏
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Clinical and Genetic Features of NPHS1 Variant-Related Nephrotic Syndrome in Chinese Children: A Multicenter, Retrospective Study

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Introduction: Few studies have addressed the genetic spectrum of NPHS1 variants in Chinese children with nephrotic syndrome. In this multicenter study, the clinical manifestations and features of NPHS1 variants in Chinese children with nephrotic syndrome were researched.

Method: Genotypical and phenotypical data from 30 children affected by NPHS1 variants were collected from a multicenter registration system in China and analyzed retrospectively.

Results: Patients were divided into two groups: congenital nephrotic syndrome (CNS [n=24]); and non-CNS (early onset nephrotic syndrome [n=6]). Renal biopsy was performed on four patients in the non-CNS group, revealing minimal change disease in three and focal segmental glomerulosclerosis in one. A total of 61 NPHS1 variants were detected, involving 25 novel variants. The “hot variants” included c.928G>A (p.Asp310Asn) in eight patients with CNS, followed by c.616C>A(p.Pro206Thr) in four and c.2207T>C(p.Val736Ala) in three. Steroid treatment was applied in 29.2% (7/24) of the patients in the CNS group and 50% (3/6) of the patients in the non-CNS group. One patient in each group experienced complete remission but relapsed subsequently. Immunosuppressants were administered to three patients in the non-CNS group, eliciting an effective response. In the CNS group, three patients underwent renal transplantation and six died mainly from infection.

Conclusion: Variants of NPHS1 gene cause CNS as well as early childhood-onset nephrotic syndrome. NPHS1 variants in Chinese individuals with NS were mainly compound heterozygous variants and c.928G>A(p.Asp310Asn) in exon 8 was a hot variant, followed by c.616C>A(p.Pro206Thr) in exon 6. Steroids and immunosuppressants may have effects in selected patients.

关键字 NPHS1, congenital nephrotic syndrome, children, multicenter, steroid resistance

分类：17. Nephrology 肾脏
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Pediatric primary sjögren syndrome presenting with renal tubular acidosis:A case report

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Objectives：By reviewing the clinical features, laboratory finding, diagnosis and treatment of children with primary sjö gren syndrome （pSS） ， we hope to raise awareness
of this rare disease among pediatricians.
Methods:The medical data was retrospectively analyzed about a patient who was diagnosed with
pSS complicated by renal tubular acidosis(RTA) in our department.
Results: A 12-year-old girl developed symptoms of cough,vomiting and hypokalemic paralysis.Tests in her local hospital showed kaliopenia(K+ 1.48mmol/L) and hyperchloremia(CI-
118mmol/L). PH values of blood and urine were 7.30 and 7.0 respectively.Based on the above
results as well as the lack of typical sicca symptom,she was diagnosed with RTA at first.
Subsequently,the patient was referred to our hospital and tested positive for anti-SSA,anti-SSB,
ANA and mycoplasma pneumoniae antibodies (Mp-Ab 1:160) . Urine analysis showed an increase
in PH value (8.0) as well as beta2-microglobulin concentration(24.430mg/L). Besides,
hyperglobulinemia(globulin 40 g/L,IgG 18.7g/L) was also found.Uneven internal echoes in
bilateral parotid glands was disclosed by ultrasound. Examnations for

Scr,ESR,RF,anti-Sm,anti-dsDNA,anti-RNP ,anti-Jo-1,anti-phospholipid,P-ANCA,C-ANCA,hepatit
is C virus,Schirmer ’ s test and tear breakup time were negative or normal.With the overall
consideration, pSS was suspected therefore the girl was required to do labial gland and renal
biopsies.Later,pathological findings revealed the lymphocytic infiltration of the salivary gland
tissue (containing＞50 lymphocytes in a section) and renal tubular interstitium,so that the
diagnosis of Sjogren's syndrome complicated with RTA was established. The girl received
prednisone 20mg/day orally along with supportive care like potassium and alkali supplement.We
also prescribed antibiotics for her in consideration of infection. The patient was discharged after
the symptoms disappeared and serum potassium returned to normal level. The reexamined titers of
MP-Ab dropped to 1:40. She was maintained on low-dose prednisone therapy during follow-up

with stable renal function.
Conclusions: Primary Sjögren syndrome is rare in children, mostly affecting middle-aged women
without exact etiology.Since it is a chronic autoimmune disease characterized by infiltration of
lymphocytes in salivary gland and lacrimal gland,xerostomia and xerophthalmia are the most
common manifestations. Kidney can be involved as well with the lesions mostly targeting the
distal tubular segments,which leads to renal tubular acidosis.Atypical symptoms and rarity of
pediatric pSS may bring a huge diagnostic challenge to clinicians. This case stressed the
importance of careful search in RTA patients onset in adolescence,especially for the female
youngsters.Pediatricians should maintain scepticism about
underlying Sjö gren syndrome.Immunological examinations should be carried out when necessary
and sometimes biopsy needs to be considered as well.

关键字 primary sjögren syndrome; renal tubular acidosis; child;case report

分类：17. Nephrology 肾脏
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Robo2 and Gen1 Coregulate Ureteric Budding through Activation of the MAPK/ERK Signaling Pathway in Mice

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Objectives: Congenital anomalies of the kidney and urinary tract (CAKUT) are one of the most common developmental defects. To explore the relationship between the superposition effect of *ROBO2* and *GEN1* genes, we established a double knockout mouse model to identify the superposition effect on the development of metanephros in mice.
Methods: The PB transposon inserted into the intron of the Gen1 and Robo2 genome to reduce the expression of the target gene in mice. Using novel Hoxb7/myr-Venus transgenic mice as a useful tool, we observed the characters of varied phenotype of CAKUT and budding of UB in all kinds of mutation (WT, $Gen1^{PB/+}$, $Robo2^{PB/+}$, $Robo2^{PB/+}Gen1^{PB/+}$) mice.
Results: 1)In the whole embryos of the $Robo2^{PB/+}Gen1^{PB/+}$ mutant mice, the expression of Robo2 decreased by 41% compared with that of the WT mice ($P<0.0001$), but the expression of Robo2 was not different from that of the $Robo2^{PB/+}$ mutant mice. In the whole embryos of the $Robo2^{PB/+}Gen1^{PB/+}$ mutant mice, the expression level of Gen1 was decreased by 53% compared with that of the WT mice ($P < 0.0001$), but the expression of Gen1 was not different from that of $Gen1^{PB/+}$ mutant mice.
2)The incidence of CAKUT in $Robo2^{PB/+}Gen1^{PB/+}$ newborn pups was 32.3%, which was higher than that in the $Robo2^{PB/+}$ group (32.3% vs.13.6%, $P=0.01$) and in the $Gen1^{PB/+}$ group (32.3% vs.17.3%, $P=0.038$). Isolated duplex kidneys were the most common anomalies in the $Robo2^{PB/+}Gen1^{PB/+}$ newborn pups, accounting for 30.2% (29/96), and the remaining 2.1% (2/96) presented hydronephrosis complicated with duplex kidneys. Five percent (1/20) of the WT newborn mice showed duplex kidneys. The incidence of duplex kidney, hydronephrosis and renal dysplasia was 4.5% in the $Robo2^{PB/+}$ neonatal mice. Thirteen percent (7/52) of the $Gen1^{PB/+}$ newborn mice showed duplex kidney, and 3.8% (2/52) of the mice showed hydronephrosis.
3)The $Robo2^{PB/+}$ and $Gen1^{PB/+}$ mutant embryos had a single UB at the typical T-stage (E11.5), whereas the $Robo2^{PB/+}Gen1^{PB/+}$ mutants frequently showed ectopic budding that had already branched from the main UB. No ectopic budding was observed in any of the 32 WT mice or in any of the 24 $Robo2^{PB/+}$ embryonic control mice. A total of 3.0% (1/33) of the $Gen1^{PB/+}$ mutant kidneys showed ectopic budding compared with 26.8% (11/41) of the $Robo2^{PB/+}Gen1^{PB/+}$ kidneys (0/32 vs 11/41, $P=0.002$; 0/24 vs 11/41, $P=0.005$; 1/33 vs 11/41, $P=0.005$).
4) Compared with that of the WT mice, the expression of Gdnf was decreased in the $Gen1^{PB/+}$ mutant mice ($P=0.03$), increased in the $Robo2^{PB/+}$ mutant mice ($P<0.001$), and significantly increased in the $Robo2^{PB/+}Gen1^{PB/+}$ mutant mice ($P<0.001$). The expression of Ret was increased in the $Robo2^{PB/+}$, $Gen1^{PB/+}$ and $Robo2^{PB/+}Gen1^{PB/+}$ ($P<0.001$) mutant mice. We detected the genes involved in the regulation of the GDNF/RET signaling axis and the cause of duplex kidney: Grem1, Bmp4, Bmp2, Six2, Foxc1, Slit2 and Sox11. Among them, Grem1 expression was increased in the $Robo2^{PB/+}Gen1^{PB/+}$ mutant mice ($P = 0.04$), while both Bmp2 and Bmp4 expression levels were decreased in the $Robo2^{PB/+}Gen1^{PB/+}$ mutant mice ($P<0.001$). Six2, Foxc1, Slit2, and Sox11 expression levels were not changed in the four groups.
5) We examined the phosphorylation of a downstream effector, ERK, pERK was increased in the UB and occasionally in surrounding cells in the $Robo2^{PB/+}Gen1^{PB/+}$ E11.5 kidneys compared with the WT ($P=0.0014$), $Robo2^{PB/+}$ ($P=0.0069$), and $Gen1^{PB/+}$ kidneys ($P=0.0015$).

We determined the level of phosphohistone-H3 (PHH3), which is an indicator of mitosis. In the Robo2$^{PB/+}$Gen1$^{PB/+}$ E11.5 kidney sections, PHH3 expression was increased compared with that of the WT ($P<0.001$), Robo2$^{PB/+}$ ($P=0.0005$), and Gen1$^{PB/+}$ groups ($P<0.001$). **Conclusions**：Robo2 and Gen1 have synergistic effects on mouse kidney development, promoting cell proliferation through activation of the GDNF/RET pathway and downstream MAPK/ERK effects. Our findings provide a disease model for CAKUT as an oligogenic disorder.

关键字 Gen1 mutation, Robo2 mutation, CAKUT, oligogenetic disease, synergistic effect, metanephros development

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An anti-ANGPTL3-FLD monoclonal antibody protects against podocytopathy and proteinuria by alleviating mitochondrial damage

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Objectives: Podocyte damage has been recognized as a crucial factor in developing multiple variants of kidney disease. Characterized by podocyte damage and proteinuria, podocytopathy is a common pathology of glomerular diseases. A mitochondrial dysfunction is an early event in podocyte damage and one of the primary mechanisms in injury and death. Our previous research showed that angiopoietin-like-3 (ANGPTL3) plays a crucial role in podocyte injury. However, its role in mitochondrial dysfunction of podocytes remains unknown. In the present study, our group developed a monoclonal antibody against ANGPTL3-FLD to explore whether this antibody can alleviate podocyte injury, in vivo and in vitro, through mitigating mitochondrial dysfunction.
Methods: A mouse anti-human ANGPTL3-FLD monoclonal antibody was generated. In addition, puromycin aminonucleoside (PAN)-treated podocytes in vitro and a mouse model of adriamycin-induced nephropathy in vivo were used to evaluate the effect of anti-ANGPTL3-FLD monoclonal antibody and related signaling in podocytopathy.
Results: Our data showed that the anti-ANGPTL3-FLD monoclonal antibody could recognize human and mouse ANGPTL3-FLD specifically. Moreover, the competitive ELISA assay demonstrated that anti-ANGPTL3-FLD monoclonal antibody could effectively block the binding between ANGPTL3-FLD and Integrin αvβ3, the EC50 is 1.57ug/ml. In vivo, mice injected with adriamycin developed massive proteinuria that peaked on day 28 and slightly subsided by day 42. Anti-ANGPTL3-FLD monoclonal antibody significantly decreased the proteinuria at the 4th week and the 8th week. Hypercholesterolemia and hypoalbuminemia were developed after adriamycin injection, which was significantly ameliorated by anti-ANGPTL3-FLD monoclonal antibody treatment. The significant podocyte injury feature-podocyte vacuolar degeneration, podocyte foot process effacement, and podocytopenia were detected in adriamycin injured kidneys. These lesions were markedly ameliorated after anti-ANGPTL3-FLD monoclonal antibody treatment. Podocyte death was further evaluated, and we found that anti-ANGPTL3-FLD monoclonal antibody treatment diminished cell death in adriamycin-injured kidneys and puromycin aminonucleoside-injured podocytes. Coincides with the results of competitive ELISA mentioned above, anti-ANGPTL3-FLD monoclonal antibody mitigated Integrin αvβ3 activation in podocytes, both in vivo and in vitro. Then, the oxidative stress was examined. Adriamycin and PAN caused robust ROS production in adriamycin-injured kidneys and PAN injured-podocytes.
In contrast, along with the amelioration of integrin β3 activation, we found a significant decrease in ROS production after anti-ANGPTL3-FLD monoclonal antibody treatment. Next, to assess whether the anti-ANGPTL3-FLD antibody attenuated oxidative stress in podocytes was ascribed to an improvement in mitochondrial dysfunction, mitochondrial morphology and function in podocytes were examined. Mitochondrial morphological abnormalities, reduced mitochondrial membrane potential, mtDNA copy number, and the upregulation of mitochondrial ROS induced by adriamycin and PAN were significantly alleviated by anti-ANGPTL3-FLD monoclonal antibody treatment. Since Integrin αvb3 mainly promotes ROS production by activating the downstream Rac1 and

Rac1 activation was associated with mitochondrial dysfunction, the expression level of Rac1 and the regulators of mitochondrial biogenesis and fusion were detected. Anti-ANGPTL3-FLD monoclonal antibody treatment significantly ameliorated Rac1-activation, restored NRF1, TFAM expression, and markedly increased Mfn1 expression but has no significant effect on the expression of Drp1, as compared to the PAN treatment group.
Conclusions: Our study demonstrated for the first time that blocking ANGPTL3 may protect the glomerulus and podocytes by enhancing mitochondrial functions and may serve as a promising therapeutic strategy for the treatment of podocytopathy.

关键字 ANGPTL3，podocytopathy，proteinuria，mitochondrial

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Detection of de novo PAX2 Variants and Phenotypes in Chinese Population: A Single-center Study

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Objective: PAX2 is a nuclear transcription factor gene highly conserved among species. Variants within PAX2 have been shown to result in optic nerve colobomas and renal hypoplasia. However, little clinical and genetic information is currently available about PAX2 variants in Chinese children. This study aimed to further understand the clinical manifestations and genetic characteristics of PAX2 variants in the Chinese population.
Methods: In this single-center retrospective study, we analyzed the clinical data of eleven children who were identified as carriers of PAX2 variants by gene sequencing. And all the variants found in this study were analyzed using in silico prediction and American College of Medical Genetics and Genomics (ACMG) standards and guidelines.
Results: The age for the development of the first symptom in 11 unrelated children was 7.4 years old. Proteinuria was found in all patients, 90.9% of children had been found bilateral renal dysplasia by renal ultrasound. Three children underwent renal pathological examination, one case showed high-intensity C1q deposition in the kidney, and the other two cases showed FSGS and mild glomerular lesions, respectively. Three children had PAX2-related ocular abnormalities, including nystagmus, retinal exudation, amblyopia, microphthalmia, microcornea, total blindness. In addition, two patients were found to have comorbidities of left renal vein entrapment and oculocutaneous albinism, respectively. Nine different PAX2 variants were found in eleven patients, four of which were reported for the first time.
Conclusion: We reported some patients with special manifestations and comorbidities, and reported four novel variants that have not been previously identified. The PAX2 gene is prone to spontaneous variants, and the outcome of the patients is unfavorable. Because of the lack of specific therapy, genetic testing should be recommended for individuals with obvious evidence of renal dysplasia and eye abnormalities and initiating renal protective therapy early.

关键字 PAX2 gene, Novel variant, Children, Renal hypoplasia, C1q nephropathy

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Townes-Brocks syndrome associated with SALL1 gene mutation: a report of 2 cases and review of the literature

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Background: Townes-Brocks syndrome (TBS) is a rare autosomal dominant congenital anomaly syndrome, which is characterized by developmental deformity of anus, limbs and external ear and hearing loss,and may have abnormal kidney. At present, some studies have shown that TBS is the result of mutation of development gene spalt-like transcription factor 1(SALL1).

Result: We reported 2 children with Townes-Brocks syndrome, both of whom started from kidney diseases, and other system malformations were found by tracing the medical history. Gene detection showed that SALL1 had nonsense mutation (c.1273C>T, p.Q425X) and SALL1 had frame shift mutation (c.1111_1121 del, p.S371Lfs*15). By reviewing the reported 28 case reports or literature review, we summarized the renal pathological data of 133 children with TBS syndrome, including 2 children in this study. Among them, 44 cases (33%) had abnormal renal function and 72 cases (54%) had abnormal renal structure, of which renal dysplasia was the main manifestation, accounting for more than 70% of all renal structural abnormalities. We also found that 7 patients had a rare phenotype-congenital hypothyroidism.

Conclusion: Two new mutation sites (c.1273C>T, c.1111_1121 del) which caused the mutation of SALL1 gene in TBS syndrome were found, and the results of pathogenicity analysis showed that they were consistent with pathogenicity variation. The clinical manifestations of TBS are highly variable. Besides the typical anal, limb and external ear deformities, renal lesions are also a common phenotype, including abnormal renal structure or function. At the same time, we found that hypothyroidism may be caused by the mutation of SALL1 gene affecting the expression of PAX8 gene, and then affecting the growth and development of thyroid.

关键字 case report, Townes-Brocks syndrome, SALL1 mutation, pediatrics

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Segmental sclerosis and mesangial proliferative glomerulonephritis in a child with branchio-oto-renal syndrome

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Objective To increase awareness of renal involvement in branchio-oto-renal (BOR) syndrome. Method To report a BOR child, missed diagnosed for 1 year, with proteinuria and presenting as segmental glomerular sclerosis and mesangial proliferative glomerulonephritis (MsPGN) in renal pathology. Result An 8-year old girl was detected proteinuria (urine protein ++), hypoproteinemia (ALB 26.9g/L) and renal insufficiency (SCr 111μmol/L) in local clinics. After traditional medicine treatment for a month, she was referred to a general hospital in which laboratory examination revealed: urine protein ++(55.6mg/kg/24hr), BUN 15.8mmol/L, SCr 87μmol/L, Chol 6.4mmol/L and cystic changes in renal ultrasound. Renal biopsy was conducted and immune complex-mediated MsPGN with segmental sclerosis was diagnosed. Blood examinations for secondary factors causing immune diseases or secondary NS were all negative. WES examination revealed no variation with sufficient pathogenic evidence; a doubtful PKHD1 variation with insufficient pathogenic evidence (PKHD1 c.4009G>A from father, PKHD1 c.7855G>T from mother); and some other variants without family verification. Autosomal recessive polycystic kidney disease (ARPKD) was also considered. Glucocorticoid (GC, Medrol 8mg Bid) and mycophenolate mofetil (MMF, 0.25g Qd) were given, which were irregularly adjusted during the following year without regular follow-up. One year later, proteinuria showed no significant relief (51.3mg/kg/24hr). She was then referred to our hospital and admitted with “MsPGN; ARPKD?” as outpatient diagnosis.
Unexpectedly, during physical examination, bilateral anterior auricular fistula was found (which appeared at birth but overlooked by her mother and not noticed by previous clinicians). There was also bilateral anterior cervical fistula. WES report was reviewed carefully and a “likely pathogenic” variant (EYA1 c.1319G>A) was redefined as “pathogenic” with added family verification and clinical evidence. Examination revealed proteinuria (39.0~68.9mg/kg/24hr), BUN 15.1~18.5mmol/L, SCr 102~119μmol/L, ALB 35g/L and Chol 10.2mmol/L. Test for C3, SLE, ANCA and etiology were all negative. MMF-AUC was 47.6 μg.hr/ml. Ultrasound showed small kidneys (Left 5.9cm×2.7cm, right 4.6cm×2.2cm). MRI revealed small renal cysts bilaterally. Renal biopsy samples were re-stained and taken reassessment with the formers: Segmental glomerular sclerosis, mild-to-moderate proliferation of mesangial cells with partial periglomerular fibrosis, multifocal tubular atrophy (~40%) with foam cells and interstitial fibrosis; IF revealed IgG+, IgM+, C3+, C1q+, depositing focally, segmentally and granularly along mesangial areas; EM showed dense deposition in subendothelial area, mesangial area and GBM. Pure tone audiometry test showed mild hearing loss in both ears. Diagnosis of BOR was clear, which might also complicated with immune-mediated glomerulonephritis. Weighing the pros and cons, MMF treatment was discontinued with GC reduced regularly. Monthly follow-up was advised while her long-term prognosis still need time to observe. Conclusion Careful physical examination is important in discovering those genetic diseases. Immunosuppressive therapy in BOR patients should be considered carefully as its disadvantages may overweigh the advantages. Moreover, we report the renal biopsy information of a BOR child, which is rare to date.

关键字 segmental sclerosis; mesangial proliferative glomerulonephritis; branchio-oto-renal syndrome

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Multisystemic manifestations in a Chinese boy with two mitochondrial DNA deletions: mitochondrial nephropathy, hypoglycemia, and pancytopenia

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Background Mitochondrial disorders are clinically heterogeneous conditions associated with dysfunctional cellular energy production arising as a consequence of oxidative phosphorylation defects. The deletion of mt DNA defect the oxidative phosphorylation pathway finally result in clinical manifestations.
Methods The proband from a nonconsanguineous Chinese family, he was diagnosed, treated, and followed up in the Department of Nephrology, Children's Hospital of Chongqing Medical University, Chongqing, China.
Results The boy was born to full-term (birth weight 3200g) and was the first child of a nonconsanguineous Chinese parents, and he was in good health before age 3 years. At the age of 3 years and 10 months old, he was admitted to the hospital because of recurrent syncope and epistaxis, his clinical manifestations involved hypoglycemia, pancytopenia, proteinuria, renal insufficiency(eGFR 20ml/min/1.73m2), inappetence, growth retardation, muscle weakness, muscle atrophy, and skeleton deformities. The electron microscopic examination of renal and muscle biopsies were reveled abnormal mitochondrial proliferation. Whole exome sequencing with mitochondrial DNA (mtDNA derived from the blood) sequencing revealed two deletions of mtDNA: ①a novel deletion of the mtDNA (deletion of m.7,617-9,953del2,336), five genes were within the deletion region, including COX II, COX III, MT-TK, ATPase 6, ATPase 8.②a 58 bp deletion (m.5,791-5,869), MT-TC and MT-TY were within the deletion region. This variant came from his mother, whereas his mother didn't have any discomfort until nowadays.
Conclusion This child diagnosed as multisystemic manifestations of mitochondrial disease due to the two deletions of mtDNA, and his clinical symptoms were different from other mitochondrial cytopathy children. The deletion has never been reported, so it has enriched the gene pool of mtDNA deletion.

关键字 mitochondrial DNA deletion, children, mitochondrial nephropathy, hypoglycemia, pancytopenia

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Hyperuricemia is correlated with the progression of IgA nephropathy in children

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Introduction: Immunoglobulin A nephropathy (IgAN) is the most common forms of primary glomerulonephritis in children. We aim to explore potential biomarkers and risk factors in IgAN children by metabolomic study.
Methods: Untargeted metabolomics analysis were performed on serum samples derived from IgAN children before and after treatments and controls. To further verify the role of hyperuricemia in IgAN children, a retrospectively study was conducted on the clinical and pathological data of IgAN children in past 15 years.
Results: The results of serum metabolites study showed that the levels of serum xanthosine (the precursor substance of serum uric acid (SUA)) were closely related to outcome of IgAN, and KEGG pathway enrichment analyses showed that differential metabolites were significantly enriched in purine metabolism. Furthermore, the retrospectively analyses of 252 IgAN children also showed that IgAN children with hyperuricemia have poor renal function and worse renal pathology. Multivariate logistic regression analysis showed that body mass index, serum creatinine, low eGFR, Lee’s grade III and crescents were risk factors of hyperuricemia in IgAN children. Multiple linear regression analysis found that high level of SUA was the risk factor affecting the progression of IgAN children.
Conclusions: We perform a dynamic metabolomics study for the first time to reveal that the level of SUA is closely related to the progression of IgAN children. Then the retrospective analyses also confirm that hyperuricemia is the risk factor for the poor renal outcome. Hyperuricemia plays an important role in the progression of IgAN children. Combined administration of uric acid-lowering therapy may help delay the progression of IgAN in children.

关键字 immunoglobulin A Nephropathy; metabonomics; hyperuricemia; children; progression

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A Novel AQP2 Gene Mutation Related Congenital Nephrogenic Diabetes Insipidus with Renal Impairment: A Case Report and Literature Review

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Backgrounds:
Congenital nephrogenic diabetes insipidus (CNDI) is a rare disorder caused by mutations in two different genes: 90% occur in the gene that codes for the vasopressin 2 receptor (AVPR2) found on the X chromosome and 10% in the gene for aquaporin-2 (AQP2) located on chromosome 12q13, characterized by failure of the kidneys to concentrate urine. Here we present the clinical diagnosis process of a case of congenital nephrogenic diabetes insipidus with kidney impairment and further studies identified a novel mutation of AQP2 gene.
Case:
A 13 years old boy was admitted to our department due to he was found over 3 weeks of renal insufficiency. There was a long history of polyuria/polydipsia for more than 10 years but without any treatment. Laboratory data before admission revealed serum creatinine 140.9μmol/L, sodium 153mmol/L, potassium 3.13mmol/L, urine protein 0.5g/L. The patient's father was diagnosed ESRD many years ago and died for esophageal cancer in 2015. Physical examination on admission: He was 151cm (-1.2SD) in height, 59kg (+1SD) in weight and BMI 25.88kg/m2 (>97th). The urine specific gravity was 1.003 and osmolality was 117mOsm/kg. Urinalysis showed urine protein was 153mg/24hr and urinary β2 microglobulin was 1.33mg/L (reference < 0.12mg/L). The blood chemistry results revealed the following levels: serum potassium 3.33mmol/L, sodium 141mmol/L, urea nitrogen 6.6mmol/L, creatinine 116μmol/L (Ccr 56.13 ml/min•1.73m2), albumin 41.7g/L and serum osmolality 294.8mOsm/kg. Renal ultrasonography showed unremarkable abnormal. Brain MRI data suggest the existence of high signal in the pituitary gland. The total urine volume output was range 3L to 7L after admission. Diabetes insipidus was suspected and an arginine vasopressin (AVP) stimulation test results were compatible with NDI. Renal biopsy revealed chronic tubulointerstitial nephritis with global sclerosis. Disease-targeted exome sequencing was performed and identified aheterozygous mutation of c.800delG, leading to a frameshift mutation in AQP2 gene which has not been previously described, suspected pathogenic on software prediction.
Conclusions: This patient with CNDI caused by a novel heterozygote mutation in the AQP2 gene, leading to a frameshift mutation, which has not been previously described, and thus expands the spectrum of the AQP2 gene mutations.
Points of discussion: Considering the diagnosis of nephrogenic diabetes insipidus in a child with polyuria/polydipsia and gene tests are recommended to identification of the AQP2 gene, as early recognition of CNDI in children especially that show only non- specific symptoms can be facilitated and renal impairment can be avoided.

关键字 AQP2; Congenital Nephrogenic Diabetes Insipidus; Renal Impairment

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Nephrolithiasis in two children with Kabuki syndrome

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Objective To expand the understanding of renal phenotype with Kabuki syndrome (KS) .KS is a multiple congenital anomalies syndrome. The five important manifestations of KS including facial dysmorphism, cardiac anomalies, postnatal short stature, mental retardation and skeletal anomalies.It had reported an incidence of urinary tract abnormalities in 28% of patients with KS. Renal involvement was usually in the form of anatomic abnormalities, but nephrolithiasis has not been described in KS. We identified 2 de dovo mutations in KMT2D gene, in the two patients, who were diagnosed as KS and presented with nephrolithiasis.
Method The clinical data of were collected, and the pathogenic mutation was detected by gene testing. Literature review to guide the clinical adjustment of treatment.
Case report Patient 1 is a 10-months-old boy born after an uneventful pregnancy. His medical history was marked with growth retardation and pulmonary hypertension caused by atrial septal defect, hypothyroidism. His renal ultrasound showed nephrolithiasis and small renal dysplasia. He was noted to have the typical facial features, including long palpebral fissures, eversion of the lower lateral eyelids, arched eyebrows with sparse lateral one-third, medial epicanthic fold, ptosis, depressed nasal tip and high palatal arch. Then, gene testing was performd. A de novo mutation (c. 6595delT, p.Y2199Ifs*65) in the KMT2D gene was identified.
Patient 2 is a 9-months-old boy was born after an uneventful pregnancy to unrelated healthy parents who originated from China. His medical history was marked with recurrent respiratory tract infection and patent foramen ovale. At 15 mo of age, 16 mo of age and 17 mo of age, he was repeatedly hospitalized with urinary tract infection. Renal ultrasound showed nephrolithiasis and bilateral mild hydronephrosis. General physical examination found that he have the typical facial features as patient1. Then, gene testing was performd. A de novo mutation (c.15113_15115 delAGG, p.E5038_G5039 delinsG) in the KMT2D gene.
Conclusion Nephrolithiasis is an important complication of KS. Based on the present cases, we hypothesized that the nephrolithiasis may be associated with the mutation in KMT2D gene.

关键字 Nephrolithiasis ， Kabuki syndrome，KMT2D gene

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HIF PHD inhibitors in CKD patients: from anemia to COVID-19

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Background: It has become clear that tissue hypoxia is a prominent feature in a range of disorders. Chronic hypoxia is the common pathology process in CKD, especially for anemia. While Hypoxemia in COVID-19 patients with diffuse lung injury is common. Hypoxia-inducible factor (HIF) is known as the central role to regulate hypoxia response. HIF-PHIs are a class of new medicines for stabilizing HIF and regulating the downstream pathway, which proved to be effective to correct anemia in CKD patients. Recently some authors speculate on the potential role of HIF PHDs as a protective agents against COVID-19.

Method: In this review, PubMed, Elsevier, and Web of Knowledge were searched for identifying relevant papers. We analyzed the literatures to assess the available evidence of HIF PHD inhibitors used in CKD patients with COVID-19 infection.

Results: In CKD patients with COVID-19 infection, HIF PHD inhibitors not only correct renal anemia, but improve the COVID-19 infection through regulating the expression of ACE2 and TMPRSS2 and other pathways.

Conclusion: HIF-PHDis could serve as a promising treatment of CKD patients with COVID-19 infection, but off-target complications should be concerned.

关键字 HIF PHD inhibitors; CKD; Anemia; COVID-19

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Clinical and prognosis analysis of children with kidney retransplantation

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Objective To analyze the clinical and prognosis of children with kidney retransplantation. **Methods** Clinical data of children who underwent kidney retransplantation from January 2011 to December 2020 in Department of Nephrology, Children′ s Hospital of Fudan University were retrospectilely avedyzed. The clinical data including demographic parameters, primary diagnosis, characteristics in the follow- up of renal allograft were analyzed. **Results** Totally 11 cases received secondary renal transplantation (male 6, female 5). They were initially diagnosed with chronic kidney disease at the age of 11.9 (7.4, 13.3) years. The median duration of dialysis was 22.1 (3.5, 36.5) months. In the first transplantation, recipient age was 13.9 (11.1, 15.2) years old. Ten cases received donation from cardiac death donor (DCD) (9 cases received donors aged less than one year and one case received donor aged one to three years) and 1 case with living- related donor. Ten graft failures occurred within 1 month after renal transplantation and the other one occurred at the fifth month after transplantation. The causes included vascular factors (9 Cases), rejection (1 Cases) and primary non- function (1 Cases). In children with graft failures, 9 donors less than one year old, and 5 of en bloc kidneys. In the second transplantation, recipient age was 14.7 (11.7, 16.2) years old. All the 11 children received dialysis (7 with PD and 4 with HD) and successfully completed the second transplantation. The median time between the two transplants was 210 (16, 1 041) days. Donors were all DCD donors from 3 years of age or older. The mean follow- up duration was (42±15) months. The estimated glomerular filtration rate was (85±34)ml/(min·1.73m2) when the last investigation after kidney retransplantation with the kidney and patient all survived. **Conclusions** Kidney retransplantation may have better prognosis in children. Dialysis transition during waiting period and DCD donor from 3 years of age or older can effectively ensure the success of kidney retransplantation.

关键字 kidney transplantation; child; kidney retransplantation

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Phenotypic spectrum and genetics of PAX2-related disorder in the Chinese cohort

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Background Pathogenic variants of PAX2 cause autosomal-dominant PAX2-related disorder, which includes variable phenotypes ranging from renal coloboma syndrome (RCS), congenital anomalies of the kidney and urinary tract (CAKUT) to nephrosis. Phenotypic variability makes it difficult to define the phenotypic spectrum associated to genotype.

Methods We performed clinical phenotyping in patients enrolled in the China national multicenter registry who were diagnosed with pathogenic variant in PAX2 and reviewed all the published cases with PAX2-related disorder. We conducted a phenotype-based cluster analysis by variant type and molecular modeling of the structural impact of missense variants.

Results Twenty different PAX2 pathogenic variants were identified in 32 individuals (27 families) with diagnosis of RCS (9), CAKUT (11) and nephrosis (12) from the Chinese cohort. Individuals with abnormal kidney structure (RCS or CAKUT group) tended to have a likely/presumed gene disruptive (LGD) variants (Fisher test, $p<0.05$). A system review of 234 reported cases to date indicated a clear association of RCS to heterozygous loss-of-function PAX2 variants (LGD variants). Furthermore, we identified a subset of PAX2 missense variants in DNA-binding domain predicted to affect the protein structure or protein-DNA interaction that associated with the phenotype of RCS.

Conclusion Defining the phenotypic spectrum combined with genotype in PAX2-related disorder allow us to predict the pathogenic variants associated with renal and ophthalmological development. It highlighted the approach of structure-based analysis can be applied into diagnostic strategy aiding precise and timely diagnosis.

关键字 Congenital anomalies of the kidneys and urinary tract (CAKUT); PAX2; renal coloboma syndrome (RCS), phenotypic cluster analysis

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Risk Factors associated with End-Stage Kidney Disease (ESKD) in children with Congenital Anomalies of the Kidneys and Urinary Tracts (CAKUT): A comparative cohort study of the Chinese Children Genetic Kidney Disease Database

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Background
Congenital anomalies of the kidney and urinary tract (CAKUT) are the leading cause of end-stage kidney disease (ESKD) in children. The aim of this study was to evaluate factors associated with ESKD and underlying genetic abnormalities in children and adolescents with CAKUT. Focusing on the severe end of the CAKUT may help identify modifiable or disease predictive factors.
Methods
The genotype and phenotype of 568 CAKUT patients were collected and analyzed based on a national multicenter registration network (Chinese Children Genetic Kidney Disease Database, CCGKDD, www. ccgkdd.com.cn) covering 27 different provinces/regions in China from 2014 to 2020. The rate of gene mutations between different clinical feature were analyzed. The renal survival was established by Kaplan-Meier curves. The risk factors for ESKD were examined via Cox proportional hazards models.
Results:
We identified a CAKUT gene mutation in 46 patients (8.1%), an abnormal copy number variation (CNV) in 19 patients (3.4 %) and a chromosomal abnormality in 4 patients (0.7%). No gene mutations were observed in patients with isolated MCDK (five patients), renal ectopia (one patient), PUJO (one patient), horseshoe kidney (three patients), and megalobladder (two patients). Patients with positive family history, extrarenal phenotype and renal hypoplasia/dysplasia (RHD) exhibited higher rates of genetic risk factors than those without (29% vs. 11%, P < 0.01; 28% vs. 6%, P < 0.01 and 20% vs. 7%, P < 0.01). Moreover, 512 patients did micturating cystourethrogram (MCU) examination, more frequently genetic risk factors were found in bilateral CAKUT patients than in unilateral CAKUT patients (12% vs. 5%, P < 0.01), and in vesicoureteral reflux (VUR) with other CAKUT than in isolated CAKUT (9% vs. 5%, P =0.08). Furthermore, there were no significant differences in concordant or discordant CAKUT, VUR grade and bilateral or unilateral VUR.
ESKD occurred in 75 (13.2%) patients during the follow-up period. Prognostic analyses with the Cox proportional hazards regression model and Kaplan-Meier survival curves further identified that RHD (HR = 2.33, 95% CI: 1.19-4.56), prenatal diagnosis (HR =2.28, 95% CI: 1.30-4.00), and Genetic factors (EYA1, GATA3, HNFB1, PAX2) (HR =2.18, 95% CI: 1.18-4.04) as an independent risk factor for the prognosis of kidney survival time.
Conclusions:
CAKUT patients with positive family, RHD, and extrarenal manifestations were significantly related to gene mutations. We recommend that CAKUT- related gene analysis be considered in cases of these patients. The present study identified that genetic factors, RHD, and prenatal diagnosis as useful prognostic factors for the kidney survival time.

关键字 /Users/jialuliu/Desktop/cakut 摘要 to jiao.docx

分类：17. Nephrology 肾脏
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Efficacy and Safety of Dapagliflozin in Children with Proteinuric Chronic Kidney Disease: A Pilot Study

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Objectives: Approximately 5-10% of paediatric nephrotic syndrome is resistant to steroids and other immunosuppressants, and up to one third of them are caused by monogenic disorder. Blockers of the renin angiotensin aldosterone system are considered as the basic treatment of nonimmune proteinuric chronic kidney disease (CKD). Recently, sodium-glucose cotransporter 2 (SGLT2) inhibitors have demonstrated benefits in reducing proteinuria and improving kidney outcomes in patients with proteinuric CKD with and without type 2 diabetes in adults1-3. The purpose of this study was to investigate the antiproteinuric effect and safety of dapagliflozin in children with nonimmune and nondiabetic proteinuric CKD.
Methods: The study was an investigator-initiated, prospective pilot study. Eligible participants were children (aged 6-18 years) with proteinuria who were unresponsive to immunosuppression therapy or diagnosed with inherited kidney disease. All the participants were required to have been receiving a stable dose of an ACE inhibitor or ARB for at least 1 month before study drug administration. Patients were excluded if they were with diabetes, orthotic proteinuria, untreated urinary tract infection, current treatment with systemic corticosteroids/calcineurin inhibitors/other immunosuppressant medications, or with evidence of hepatic disease. After enrolment, patients were prescribed dapagliflozin 5 mg per day (bodyweight ≤30 kg) or 10 mg per day (bodyweight＞30 kg) for 12 weeks. The efficacy of dapagliflozin in lowering proteinuria was assessed by the percentage change in daily protein excretion over 12 weeks of treatment relative to baseline. This pilot study was registered at clinicaltrials.gov (NCT 04534270) and was approved by the ethical committee of Children’s Hospital of Fudan University. All patients or their legal guardians provided written informed consent before study related procedure commenced.
Results: Between June 1, 2020 and Dec 1, 2020, we screened 15 patients, and 9 of them were enrolled. One patient was lost to follow-up. Patient had a mean age of 10.36 years, a mean weight of 34.87 kg. The primary kidney disease diagnoses among them were Alport syndrome (n=5), Dent disease (n=1) and others (n=3). Among them, 6 (66.6%) patients had a previous kidney biopsy and 9 (100%) experienced gene test and confirmed their primary disease. Dapagliflozin treatment led to significant reductions in 24h proteinuria levels both at 4 weeks and 12 weeks versus baseline (1.56±0.76 vs 2.45±1.60 g/m2; 1.87±1.12 vs 2.45±1.60 g/m2; $p<0.05$, respectively). The percentage change of 24-h proteinuria from baseline was decreased by 33.25% (95% CI 23.09 to 43.41) at 4 weeks of treatment and 22.59% (95% CI 8.29 to 36.88) at 12 weeks (Fig. 1A). Although there was no significant change in plasma albumin levels at 4 weeks (37.21±5.68 vs 35.29±6.68 g/l, $p>0.05$), the plasma albumin level was increased significantly at 12 weeks compared with baseline (37.48±7.9 vs 35.29±6.68 g/l, $p<0.05$) (Fig. 1B). No significant change of eGFR was observed at 4 weeks (108.2±39.7 vs 109.2±31.9 ml/min/1.73m2, $p>0.05$), whereas it decreased slightly at 12 weeks compared with baseline (104.1±27.6 vs 109.2±31.9 ml/min/1.73m2, $p=0.048$) (Fig. 1C). The BMI remain stable during the 12 weeks treatment period (Fig. 1D).

Conclusions: The results provide a new option for the nonimmune proteinuric CKD in children, especially for the multi-drug resistant nephrotic syndrome and monogenetic kidney disease. In our limited experience, dapagliflozin is safe and effect for use in children with proteinuric CKD with an eGFR greater than 60ml/min/1.73m2. Further research involving a larger number of patients and a longer duration of treatment are necessary to confirm the efficacy of dapagliflozin in mitigating proteinuria and in slowing CKD progression in children.

关键字 Dapagliflozin Children Proteinuria

分类：17. Nephrology 肾脏
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Mutations of IFT-A subunits in children with nephronophthisis

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Objectives: Nephronophthisis (NPHP) is an autosomal recessive cystic kidney disease, which is one of the common causes of end-stage renal disease (ESRD) in children and adolescents. NPHP is caused by defects in primary cilia which serves as cellular antennae by sensing the extracellular environment, by transducing developmental signal. The IFT-A complex, comprised of 8 proteins, plays an important role in cilium transport. This study focuses on the 8 genes related to the IFT-A, aims to find novel pathogenic variants in children with NPHP.
Methods: Trio exome sequencing (Trio-ES) was performed to screen the pathogenic variants of IFT-A complex related genes in the cohort of Chinese children with NPHP from Chinese Children Genetic Kidney Disease Database, CCGKDD). Function study on human renal tubular epithelial cells (HK2) was underwent to elucidate the molecular mechanism of pathogenetic variants in IFT-A subunits.
Results: In the seven children with NPHP, biallelic pathogenic variants of *IFT122*, *IFT140*, *IFT144* (*WDR19*) and *IFTAP* (*C11ORF74*)] were detected respectively. In silico analysis for prediction of pathogenesis in the variants was performed. A total of 12 pathogenic variants were identified, including 2 homozygous mutations. And all of the pathogenic variants hadn't been reported before. Among these genes, *IFTAP* was a novel gene that could cause the occurrence of NPHP. The renal phenotypes included proteinuria, renal damage and renal cysts. We also found the extrarenal phenotypes including fundus retinitis pigmentosa, hearing loss, scoliosis, psychomotor retardation and submandibular rhabdomyosarcoma. In the experiments of HK2 cells in vitro, we observed that the length of primary cilia in cell with *IFT122*, *IFT140*, *IFT144* or *IFTAP* knockdown was significantly shorter than that in the control group through immunofluorescence staining ($P < 0.05$, t test). And, the immunofluorescence showed that IFTAP and IFT122 were located on the primary cilia. The cilia length of HK2 cells with variants of *IFTAP* or *IFT122* was shorter than that of control cells ($P < 0.05$, t test). In addition, we observed abnormal localization of BBS9 in *IFT122* knockdown cells and abnormal localization of IFT140 in *IFTAP* knockdown cells ($P < 0.05$, t test).
Conclusions: Screening pathogenic variants in IFT-A subunits such as IFT122, IFT140, IFT144 or IFTAP can establish the monogenetic cause of NPHP with the deficiency of cilium. Screening of IFT-A complex related mutations based on WES will speed up the precise diagnosis and typing of NPHP. Further genetic and functional studies will shed light on the mechanism of NPHP.

关键字 NPHP, IFT-A，Genotype, Phenotype

分类：17. Nephrology 肾脏
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A Novel CNN-Based Computer-aided Diagnostic System of Tc-99m DMSA renal scintigraphy for Early Prediction of Vesicoureteral Reflux

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Bcakgroud:
Established Deep Learning (DL) -based 99MTC-dimercaptosuccinic acid (DMSA) and other indicators of Vesicoureteral reflux VUR) prediction model.
Method:
A retrospective analysis was performed to summarize the medical text data and imaging data of 195 infants with febrile urinary tract infections who visited the Pediatric Hospital of Fudan University between 2016 and 2018. Age, gender, and the presence of a plaque in the first diagnosis of Acute Pyelonephritis APN), kidney, bladder ultrasound condition, left kidney function value, right kidney, double kidney difference, left kidney function value than the right kidney, right kidney function value than the left kidney, score on the left kidney, the left kidney under a grade, on the right kidney, right kidney under score, four scores and, first option on the left side of the VUR level, level of first option on the right side of VUR and VUR severity classification (Rating 012 as mild and 345 as severe). DMSA images of both kidneys are referred to as image data, including images of the patient's left and right kidneys.
195*2=390 samples were obtained according to the separation of the left and right kidneys. According to the severity, 204 samples were classified into the mild category (category 0) and 186 samples were classified into the severe category (category 1). Since the application of machine learning model involves two stages of model training and prediction, all 390 samples need to be divided into training data and test data.
In the experiment, in order to maintain the balance between the training set and the sample categories in the test set, the data partition results are as follows: there are 312 samples of training data, of which there are 163 samples of class 0, accounting for 52.24% of the training set, and 149 samples of class 1, accounting for 47.76% of the training set. There were 78 samples of test data, among which 41 samples of class 0 accounted for 52.56% of the test set, and 37 samples of class 1 accounted for 47.44% of the test set.
In order to compare the predictive performance of different models and analyze the influence of data information on the model to judge the severity of VUR, four sub-experiments were set up in the model group of the experiment, which respectively applied Random Forests, RF, SVM and Convolutional Neural Networks are used to model the text data. The mlP-CNN combined model (Multilayer perceptron-convolutional Neural Network) is applied to model the text and image data. The published DMSA four-zone scoring method was used as the control group of the model group to analyze the advantages and disadvantages of the model prediction and scoring method, and the F1 value of the prediction model was used as the main evaluation index.
Results:
From the index of F1 value, in the machine learning model and the traditional quadrangling scoring method, all kinds of machine learning models are better than the

traditional scoring method on the test data set. Among them, MLP-CNN model has the best identification effect for VUR severity.
According to the internal model comparison, the CNN model requires a large amount of data, which leads to its poor performance in the case of small samples, and its model performance is not as good as random forest and support vector machine.
Conclusions:
DMSA text image prediction system based on deep learning has significantly improved the prediction performance of high-level VUR compared with previous scoring methods, providing a new idea for early prediction of high-level VUR.

关键字 Convolutional Neural Network, Tc-99m DMSA , Vesicoureteral reflux

分类：17. Nephrology 肾脏
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Juvenile nephronophthisis: a case report

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Abstract
Objective: nephronophthisis is a rare congenital kidney disease, we report and analyze the clinical and pathological features of a case of juvenile nephronophthisis.
Methods: A 12-year-old boy was initially referred to the Department of Nephrology at the Children's Hospital, Zhejiang University School of Medicine due to unknown elevated serum creatinine. Gene testing and renal biopsy were carried out, clinical and pathological data were collected.
Results: 1. A 12-year-old boy went to the Department of Endocrinology and found elevated serum creatinine, he denied any history of kidney diseases.2. Laboratory tests showed proteinuria, hyperuricemia, kidney dysfunction, and magnetic resonance examination showed small cysts of both kidneys.3. Histology of the patient’s kidney under light microscopy showed proliferative sclerosing glomerulonephritis. Electron microscopy showed glomerular basement membrane segmental thickening and foot process fusion extensive. High throughput gene sequencing showed there that there was a large homozygous deletion of the NPHP1 gene on chromosome 2.
4. Conclusion: 1. Nephronophthisis is an autosomal recessive disease, which is caused by NPHP gene mutation. The disease morbidity concealment and has no characteristic clinical manifestations in the early stage. For children with growth retardation, it is recommended to take renal function and urine tests in the early stage.2. For children with chronic kidney disease, genetic testing is recommended to prevent missed diagnosis and misdiagnosis.

关键字 NPHP1; Chronic Kidney Disease; Growth Retardation

分类：17. Nephrology 肾脏
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Sotos syndrome combined with renal stones: a case report and literature review

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Abstract: Objective To summarize the diagnosis and treatment of Sotos syndrome caused by heterozygous deletion variation of NSD1 gene. Methods The clinical data of a child with Sotos syndrome complicated with double kidney stones were retrospectively analyzed, and the literature on Sotos syndrome was systematically reviewed. Results A 1 year old male child, because of recurrent urinary tract infections with double kidney stones and kidney seeper, growing tall, special appearance, mental retardation, eye strabismus of alternate external oblique 20 to 25 degrees, tremor eye level, blood pressure without exception, without special medical history and mother because of how history of ovary, children for ivf. Gene microarray showed heterozygous deletion in 5q35.2-Q35.3, in which NSD1 was located in the key pathogenic region of Sotos syndrome, and ACMG score was pathogenic mutation. The child was diagnosed as Sotos syndrome with kidney stones. Conclusion We should pay attention to the growth and development of Sotos syndrome, the evaluation and follow-up of nervous system, urinary system, cardiovascular system and eye system, control urinary tract infection, monitor the change of stone and protect renal function.

关键字 Sotos syndrome; NSD1 gene; renal stones

分类：17. Nephrology 肾脏
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Clinical and pathological characteristics in children with IgA nephropathy and dyslipidemia

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Background:
IgA nephropathy (IgAN) is a leading cause of chronic kidney disease (CKD), which is commonly accompanied by dyslipidemia. However, the intrinsic relationship between dyslipidemia and primary IgAN in children remains to be elucidated. The study aimed to investigate the impact of different types of dyslipidemia on clinical and pathological characteristics in children with IgAN.
Methods:
In this cross-sectional study, a total of 276 children with primary IgAN from January 2006 to January 2021 were included. The clinical and pathological features of different types of dyslipidemia were analyzed. Logistic regression analysis was performed to analyze risk factors for dyslipidemia and CKD stage ≥3.
Results:
A total of 185 cases (67.0%) were in the dyslipidemia group, which were divided into the hypercholesterolemia group (66 cases, 35.7%), hypertriglyceridemia group (16 cases, 8.7%), mixed hyperlipidemia group (84 cases, 45.4%) and low high-density lipoprotein cholesterol (HDL-C) group (19 cases, 10.3%) according to clinical classification, and 32.6% of children with IgAN had hypertension in our center. Children in the dyslipidemia group had higher body mass index (BMI), blood urea nitrogen (BUN), serum uric acid (SUA), and 24-h proteinuria; a higher proportion of hypertension and CKD stage ≥3; and a lower level of serum albumin and estimated glomerular filtration rate (eGFR). In addition, a higher proportion of Lee grade IV-V, E1 (endocapillary hypercellularity present), S1 (segmental sclerosis or adhesions present) and C2 (cellular or fibrocellular crescents present in ≥25% of glomeruli) was found in the dyslipidemia group. Furthermore, the clinical and pathological characteristics of children with IgAN were the worst in the mixed hyperlipidemia group. Multivariate analysis showed that hypertension, low levels of serum albumin, proteinuria ≥1 g/d per 1.73 m^2, high BMI and the presence of S1 were independent risk factors for dyslipidemia in children with IgAN. CKD accompanied by hypertension, HDL-C ≤1.04 mmol/L and increased BUN were independent risk factors for CKD stage ≥3 in children with IgAN.
Conclusions:
Children with IgAN and dyslipidemia, especially mixed hyperlipidemia, are prone to more severe clinical manifestations and pathological changes. Our study provides further insight into dyslipidemia as a potential risk factor in children with IgAN.

关键字 Dyslipidemias; IgA nephropathy; Risk factors; Children

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The efficacy and safety of calcineurin inhibitor versus mycophenolate mofetil in pediatric steroid-resistant nephrotic syndrome: a single-centre retrospective study

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【Abstract】Objective: To compare and evaluate the efficacy and safety of calcineurin inhibitors (CNIs) and mycophenolate mofetil (MMF) in children with steroid-resistant nephrotic syndrome (SRNS). Methods: A single-centre retrospective study was conducted with52 pediatric SRNS patients (including 36 boys and 16 girls) recruited in Shenzhen Children's Hospital from January 2015 to October 2020 as the main research object, whose age ranged from 1 to 16 years. All SRNS patients were divided into CNIs group (34 cases) and MMF group (18 cases) with age and sex match in the two groups on the basis of prednisone treatment. Follow-up interview was conducted regularly for one year. Clinical efficacy indicators including total remission rate, 24-hour urine protein, urinal protein-to-creatinine ratio, plasma albumin, serum creatinine, cholesterol, and adverse reaction rate, were collected from the two groups before treatment and after 6/12 months of treatment. Independent sample t test and pearson’s $\chi 2$ test were used to compare the two sets of data in this study. A $P<0.05$ value represents that the difference is statistically significant.
Results: (1) Total remission rate of CNIs group was higher than that of MMF group after six months (CNIs: CR 35.29%, PR 64.71%; MMF: CR 44.44%, PR 50.00%;), while total remission rate of CNIs group was lower than that of MMF group after twelve months (CNIs: CR 35.29%, PR 50.00%; MMF: CR 50.00%, PR 38.89%;), although no significant differences of total remission rate were found between the two groups after 6 or 12 months by statistical analysis ($P>0.05$).
(2) Upon treatment, the 24-hour urine protein and urine protein-to-creatinine ratio in both two groups significantly decreased after 6 and 12 months ($P<0.05$), as plasma albumin increased remarkably after 6 and 12 months in the two groups($P<0.05$), respectively. Except that level of serum creatinine in MMF group reduced after treatment ($P<0.05$), no significant changes of serum creatinine and cholesterol were found in the two groups after 6 and 12 months of treatment ($P>0.05$).
(3) A significant higher total remission rate was found in patients of MCD type compared with other pathological types(ESGS and MsPG) in CNIs group after 12 months of treatment (100% vs 77.78% vs 0%, $P<0.05$), while increasing trends of total remission rate and complete remission rate were found in patients of FSGS compared with MCD type in MMF group after 12 months of treatment (TR:100% vs 66.67%, $P=0.429$; CR: 75.00% vs 33.33%, $P=0.486$), respectively. Noteworthily, MMF therapy led to a higher complete remission rate in patients of FSGS type against CNIs after 12 months of treatment, although there is no significant difference of complete remission rate detected between the two treatments (75% vs 44.44%, $P=0.559$).
(4) Upon treatment, 8 children in CNIs group and 4 children in MMF group experienced adverse reactions after 6 and 12 months. No statistical differences of the incidence rate and distribution of adverse reactions were found between the two groups [incidence rate: 23.53% vs 22.22%; CNIs: gastrointestinal reaction 50%, hairy 12.5%, gingival hyperplasia 25%, hyperuricemia 12.5%; MMF: gastrointestinal reaction 75%, upper respiratory tract infection 25%; all $P>0.05$).

Conclusion: Our results indicated that both CNIs and MMF were effective in the treatment of children with steroid‐resistant nephrotic syndrome. CNIs was superior to MMF in a short course of treatment (up to 6 months), but there was a relatively uncertain efficacy between the two groups for a long course of treatment (up to 12 months). Based on data about long-term total remission rate and complete remission rate, MMF may be the preferred choice for patients of FSGS compared with CNIs which is more suitable for MCD type. Although CNIsand MMF were tolerant for most patients, more conspicuous toxicity of CNIs should be monitored closely.

关键字 steroid‐resistant nephrotic syndrome; children; calcineurin inhibitor; mycophenolate mofetil

分类：17. Nephrology 肾脏
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Renoprotection with Sodium-glucose cotransporter-2 inhibitors in children: Known and unknown

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Background Sodium-glucose cotransporter-2 (SGLT2) inhibitors represent novel hypoglycemic drugs for the treatment of adult diabetes that have shown considerable potential for cardioprotection and renoprotection. Several studies have confirmed the protective effects of SGLT2 inhibitors on the kidneys of adult diabetic patients and those with non-diabetic nephropathy, however, limited researches are seen in pediatric patients.
Method In this review, we have summarized the mechanisms of action of SGLT2 inhibitors, the current experiences in adults, results of exploratory studies in children, and adverse events & obstacles of pediatric use. We further explore the potential and possible future research direction of SGLT2 inhibitors in pediatric diseases. PubMed and Elsevier were searched for identifying relevant papers.
Results Lots of adult studies have demonstrated the significant role of SGLT2 inhibitors in type 2 diabetes, diabetic nephropathy, and non-diabetic nephropathy. The efficacy and safety of SGLT2 inhibitors are satisfying. The pharmacokinetic and pharmacodynamic studies in pediatric patients with type 2 diabetes have laid the foundation of phase-III pediatric studies. However, there are still some hurdles to overcome, including recruitment, clinical follow-up and financial support.
Conclusions Although there are still some problems remaining in the clinical application of pediatric diseases, based on the current experience of adult, it is inevitable that SGLT2 inhibitors will benefit pediatric patients in the near future.

关键字 SGLT2 inhibitors; current experiences; renoprotection;pediatric diseases

分类：17. Nephrology 肾脏
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Reduction in peritonitis rates by 20 times: 18-year results from the most active pediatric peritoneal dialysis center in China

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Background Most of the available epidemiological data on peritonitis have been derived from developed countries. Limited data from China have been reported.
Methods An 18-year (2001-2018) peritoneal dialysis (PD) program at Children's Hospital of Fudan University, with the greatest number of children on PD in China, was described and data on peritonitis were retrospectively analyzed.
Results Since 2001, a program with a comprehensive PD care-bundle has been developed and 283 patients (53.7% male, median age = 9.3 years, range 0.5-17.0) who were distributed in 76.5% of the Chinese administrative divisions were enrolled between 2001 and 2018, with an overall death rate of 3.67 per 1,000 patient-months on PD. Among these patients, 117 peritonitis episodes occurred in 68 (24.0%) patients over 4,896 patient-months. The incidence of peritonitis decreased 20-fold from 2.2 episodes per patient-year in 2003 to 0.11 in 2018, despite a 15-fold increase in the number of incident patients from 2001-2006 to 2013-2018. The median time to the first episode of peritonitis was 224 days, and the 1-year peritonitis-free survival rate was 91.0%. The culture negative rate decreased from 68.7% during 2001-2006 to 18.5% during 2013-2018, and the proportion of gram-negative and fungal infections increased significantly from 6.6% to 33.8% and 0 to 9.2%, respectively ($p<0.001$). Short stature as height ≤-2 SD (OR: 2.35, 95% CI 1.76-6.49, $p=0.005$) and PD duration≥1 year (OR: 3.38, 95% CI 1.30-4.24, $p<0.001$) was independently associated with a higher risk of developing peritonitis. Of the 117 peritonitis episodes, 9.4% required permanent removal of the catheter, among which half were fungal infections. Patients with peritonitis had a higher risk for PD technique failure ($p=0.006$), but there was no difference in estimated patient survival rates and no patient death due to peritonitis.
Conclusions Peritonitis rates have tremendously reduced in the most active pediatric PD center in China during the last 18 years. The overall outcome is good, but fungal infections, growth deficit and PD duration should be further closely monitored to maintain a low peritonitis rate.

关键字 腹膜炎

分类：17. Nephrology 肾脏
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Assessing of the impact of unclassified variants in causative genes that lead to Alport syndrome

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Objective A large number of unknown significance or unclassified variants in three COL4A3, COL4A4 and COL4A5 genes leading to Alport syndrome pose a challenge for genetic diagnosis and subsequent genetic counseling. The aims of this study were to analyze the pathogenicity of unclassified variants in the above genes and to make genetic diagnosis of Alport syndrome. **Method** The patients clinically diagnosed or suspected of Alport syndrome with unknown significance intronic cryptic sites variants and exon variants in the causative genes detected by high throughput exome sequencing were enrolled in the study. To assess the impact of these variants on splicing, the mRNA was extracted from patient-derived urine pellets directly and analyzed by reverse-transcription polymerase reaction (RT-PCR) and direct sequencing. Meanwhile, 3 in silico splicing prediction tools including HSF, NNSplice, and NetGene2 were used to evaluate whether an effect on RNA splicing was expected for these six variants. **Results** Four patients with Alport syndrome and two patients suspected of Alport syndrome were included in this study. Among these patients, two carried COL4A3 intronic cryptic sites variants and the four carried COL4A5 unclassified intronic cryptic sites variants or exon variant. Transcript analyses using patient-derived urine pellets revealed these five unclassified intronic variants and one unclassified exon variant affect RNA splicing. Taken together, six patients in this study were genetic diagnosed with Alport syndrome. The predicted effect on RNA splicing of these variants was not complete consistent using HSF, NNSplice and NetGene2. **Conclusions** The pathogenicity of unknown significance intronic cryptic sites variants and exon variant in causative genes of Alport syndrome can be determined using patient-derived urine mRNA, which provides evidence for molecular diagnosis and subsequent genetic counseling in the clinical settings.

关键字 Alport syndrome, unclassified variant, urine mRNA, molecular diagnosis

分类：17. Nephrology 肾脏
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Risk Factors for Breakthrough Urinary Tract Infection in Children with Vesicoureteral Reflux Receiving Continuous Antibiotic Prophylaxis

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Abstract
Objective: To investigate the risk factors for breakthrough urinary tract infection (BT-UTI) in children with vesicoureteral reflux (VUR) receiving continuous antibiotic prophylaxis (CAP).
Methods: This was a single-centre cohort study (January 2016 - December 2019). The clinical data of 256 children with grade I-V VUR receiving CAP were analysed. In this study, exposure variables were sex, younger age at the initial diagnosis of UTI ≤ 12months, high-grade VUR, bilateral VUR, aetiology, presence of renal scarring at the initial diagnosis, presence of renal function impairment at the initial diagnosis, ultrasound abnormalities, antibiotic used and bowel dysfunction (BBD). Outcome was BT-UTI.
Results: BT-UTI occurred in 81 out of 256 children with grade I-V VUR who received CAP, an incidence of 31.64%. Univariate analysis showed that younger age at the initial diagnosis of UTI (≤ 12 months) , bilateral VUR, renal scarring on the dimercaptosuccinic acid (DMSA) scan at the initial diagnosis of UTI and bladder and bowel dysfunction (BBD) were correlated with the occurrence of BT-UTI. Multivariate analysis showed that younger age at the initial diagnosis of UTI (≤ 12 months) (HR: 4.629, 95% CI: 1.302 - 16.462), bilateral VUR (HR: 2.078, 95% CI: 1.084 - 4.022) and BBD (HR: 3.194, 95% CI: 1.243 - 8.206) were independent risk factors for the occurrence of BT-UTI.
Conclusion: For VUR children receiving CAP, younger age at the initial diagnosis of UTI (≤ 12 months), bilateral VUR, and BBD were independent risk factors for the occurrence of BT-UTI.

关键字 Vesicoureteral reflux, continuous antibiotic prophylaxis, breakthrough urinary tract infection, children, bladder and bowel dysfunction

分类：17. Nephrology 肾脏
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Multidisciplinary Approach to Screening and Management of Children with Fabry Disease: Practice at a Tertiary Children's Hospital in China

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Background: Fabry disease (FD) remains poorly recognized, especially in children in China. Considering the diversity and non-specific clinical manifestations and life-threatening aspect of this disease, methods to improve an effective screening and management of the suspects, are needed. This study aims to explore how it can be done

effectively, in a multidisciplinary perspective for children with FD at a tertiary children’s hospital in China.
Methods: A multidisciplinary team (MDT) of pediatric FD was launched at Children’s Hospital of Fudan University. Children with high-risk portrait were referred by MDT screening team using dried blood spot (DBS) triple-test (α-galactosidase A, globotriaosylsphingosine, GLA gene). For newborns who were undergoing genetic testing in the hospital, GLA gene was listed as a routine analysis gene. Evaluation, family screening and genetic counseling were implemented after screening by MDT management team.
Results: Before the establishment of the MDT, no case was diagnosed with FD in the hospital. However, twelve-month following the MDT program's implementation, thirty-five children with high-risk portrait were referred for screening by DBS triple-test, with a yield of diagnosis of 14.3% (5/35). These 5 diagnosed children were referred due to high-risk portrait of pain accompanying with dermatological angiokeratoma and hypohidrosis (n=2), pain accompanying with abnormal liver function (n=1), pain only (n=1) and unexplained renal tubular dysfunction (n=1), respectively. Two neonates were early detected with GLA mutations in the hospital, with a yield of detection of 0.14% (2/1420). Furthermore, another 3 children diagnosed with FD were referred from other hospitals. Family screening of these 10 diagnosed children indicated that 9 boys inherited from their mothers and 1 girl from her father. Four of them started to receive the enzyme replacement therapy.
Conclusion: Screening and management of children with FD is effective based on a defined screening protocol and a multidisciplinary approach. We should pay more attention on the high-risk portraits of pain, angiokeratoma, decreased sweating, and unexplained chronic kidney disease in children.

关键字 Fabry disease, Multidisciplinary team, Rare disease, Screening, Dried blood spot, Enzyme replacement therapy, Children

分类：17. Nephrology 肾脏
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Risk factors for progression of chronic kidney disease with glomerular etiology in hospitalized children

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Aim To Identify association between risk factors to Chronic kidney disease (CKD) stage 5 in children with glomerular diseases in children in China.
Methods The Hospital Quality Monitoring System database was used to extract data for the study cohort. The primary outcome included progression to CKD stage 5 or dialysis. Cox regression was used to assess potential risk factors. Patients with lower stages (CKD stage 1 and 2) and higher stages (CKD stage 3 and 4) at baseline were analyzed separately.
Results Of 819 patients, 172 (21.0%) reached the primary outcome during a median followed-up of 11.4 months. In the lower stages group, factors associated with the primary outcome included older age (Hazard Ratio [HR], 1.21; 95% confidence interval [CI], 1.10–1.34) and out-of-pocket payment (HR, 4.14; 95% CI, 1.57–10.95). In the higher stages group, factors associated with the primary outcome included CKD stage 4 (HR, 2.31; 95% CI, 1.48–3.62) and hypertension (HR, 1.99; 95% CI, 1.29–3.07). The medical migration rate was 38.2% in this study population.
Conclusion There are different risk factors for progression to the primary outcome in different stages in CKD with glomerular etiology. Further prospective studies are needed to assess these risk factors. The high medical migration rate reflected the regional disparities in the accessibility of pediatric kidney care between regions.

关键字 Chronic kidney disease, dialysis, disease progression, hypertension, risk factor

分类：17. Nephrology 肾脏
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Association of insurance status with chronic kidney disease stages in hospitalized children

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Background Access to care with adequate insurance may be associated with earlier diagnosis, expedited treatment, and improved prognosis in chronic kidney disease (CKD).
Objective To examine the extent to which insurance is associated with access to timely diagnosis and stages differences of CKD among a large population of Chinese children.
Methods This retrospective, cross-sectional study used data from the Hospital Quality Monitoring System on 10274 children aged 0-17 years who were diagnosed as CKD stage 1 to 5 between June 1, 2013, and December 31, 2018.
Main outcomes and measures The primary outcome was advanced stage of CKD at diagnosis (defined as a diagnosis of CKD stage 4 or 5).
Results A total of 10274 children (median [Interquartile Range] age, 12.4 [7.9, 15.4] years; 5544 insured and 4730 uninsured) were included in the study. A higher proportion of children uninsured received a diagnosis of the advanced stage of CKD (stage 4 or 5) compared with children insured (46.3% vs 45.8%). In a multivariable models adjusted for age, sex, cross-regional hospitalization, year of diagnosis, and cause of CKD, uninsured children had higher odds of receiving a diagnosis of an advanced stage of CKD (odds ratio [OR] 1.20, [95%CI, 1.08-1.34]) compared with insured children.
Conclusions This study suggest that medical insurance coverage was associated with an earlier diagnosis of CKD.

关键字 chronic kidney disease, insurance, early diagnosis

分类：17. Nephrology 肾脏
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The Spectrum and Changes of Biopsy-Proven Kidney Diseases in Chinese Children

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Aim
The study aimed to investigate the spectrum of biopsy-proven kidney disease in Chinese children, analysis the trend of changes from 2004 to 2018 and the underline reasons.
Methods
A cross-sectional analysis of discharge records from the national discharge database in China was carried out. Hospital discharge records of 21515 children under 18 years old from 238 hospitals with biopsy-proven kidney disease from June 1, 2013, to December 31, 2018 were included. Variables included age, sex, year of biopsy, diagnosis before kidney biopsy, discharged diagnosis including kidney histologic diagnosis were collected. The composition of pediatric kidney disease in different sexes, age groups, and clinicopathologic correlations were accessed. The changing patterns of biopsy-proven glomerulopathies from 2004 to 2018 and the underlying reasons were anayysed.
Results
Glomerular disease made up 98.22% (21132/21515) of the total biopsy-proven kidney diseases. Henoch-Schonlein purpura nephritis (HSP) (28.77%, 6190/21132) was the most frequent pathological finding among glomerular diseases, followed by immunoglobin A nephropathy (IgAN) (22.48%, 4837/21132), minimal change disease (14.90%, 3206/31132) and lupus nephritis (10.87%, 2338/21132). Nephrotic syndrome was the most frequent diagnosis before biopsy (24.09%, 5183/21515). Tumor (50.00%, 30/60)was the most common histological finding in kidney biopsy in children less than 1 years old. Compared with previously reported results, the proportion of HSP and IgAN in glomerular disease increased significantly, whereas the proportion of minimal change disease, hepatitis B nephritis and membrane nephropathy decreased significantly during the period from 2004 to 2018.

Conclusions
The spectrum of glomerular disease among children has changed substantially from 2004 to 2018. This trend might be associated with change of preference for kidney biopsy caused by the publications of a series of guidelines on kidney disease, change of disease incident and other factors which are needed for further study.

关键字 biopsy, kidney disease, clinicopathologic correlations, glomerular disease

分类：17. Nephrology 肾脏
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Rituximab, cyclophosphamide, and tacrolimus as first steroid-sparing agent in childhood-onset, complicated frequently relapsing/steroid-dependent nephrotic syndrome and evaluation of health-related quality of life

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Abstract
Background Frequently relapsing/steroid-dependent nephrotic syndrome (FRSDNS) leads to steroid toxicity, impairing health-related quality of life (HRQOL) thus prompting the use of so-called steroid-sparing drugs. This study evaluated the effectiveness and safety of rituximab, cyclophosphamide, and tacrolimus as first-line steroid-sparing agents and their impact on HRQOL in children with FRSDNS.
Methods In total, 51 children with FRSDNS not previously treated with steroid-sparing agents, between 2019 and 2020, were equally divided to receive rituximab (single-dose of 375 mg/m2), or cyclophosphamide, or tacrolimus, along with tapering off prednisolone. Before and after these drugs, clinical findings and side effects were evaluated. HRQOL was assessed using PedsQL™ 4.0 Generic Core Scales.
Results The mean relapse rate in all groups declined 6 months after treatment ($P < 0.05$). Median time to first relapse was 17 months with rituximab, longer than 5.1 months and 9.6 months with cyclophosphamide and tacrolimus, respectively. The 12-month risk of relapse, the relapse rate, and the cumulative prednisolone dosage (53.2, 101.7, 119.2 mg/kg) were lower with rituximab than tacrolimus and cyclophosphamide ($P < 0.05$). Although all treatments were well tolerated, mild to moderate infections were twice as common in the cyclophosphamide group ($P < 0.001$). At 1 year after treatment, total, psychological health summary, and social and school functioning score improved in rituximab group compared to the other groups ($P<0.05$).
Conclusion Rituximab is more effective than cyclophosphamide and tacrolimus and safe as first-line steroid-sparing agent in children with FRSDNS, and can improve HRQOL, especially psychological, social, and school functioning.

关键字 Rituximab • Tacrolimus • Cyclophosphamide • Frequently relapsing/steroid-dependent nephrotic syndrome • Health-related quality of life

分类：17. Nephrology 肾脏
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Genotype-phenotype analysis and prognosis with primary distal renal tubular acidosis

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【Abstract】

Objective A certain basis was provided for the clinical diagnosis and treatment of primary distal renal tubular acidosis (dRTA) . As well as to determine whether genotype has associations with phenotype and the prognosis of primary distal renal tubular acidosis .

Method We conducted a retrospective case-control study involving 27 patients with distal renal tubular acidosis diagnosed in Children's hospital of Chongqing Medical Uuniverstiy in the past ten years. Clinical, genetic and follow-up data was collected.

Results The mean age at onset of 27 children with dRTA was 33.8 (33.8±41.2) months, and the mean age at diagnosis was 46.9 (46.9±42.4) months. The ratio of male to female was 16:11. Among the patients, 22 cases (81%) had *SLC4A1* gene mutations, 3 cases (11%) had *ATP6V0A4* gene mutations, and 2 cases (7%) had *ATP6V1B1* gene mutations.There was no differences between three genotypes in clinical manifestations of renal tubular acidosis. 16 patients (73%) in the *SLC4A1* group, 3 patients(100%) in the *ATP6V1B1* group, and 2 patients (100%) in the *ATP6V0A4* group were found hard to thrive. 14 patients (64%) in the *SLC4A1* group, 2 patients (67%) in the *ATP6V1B1* group had rickets, and 2 patients in the *ATP6V0A4* group did not manifest rickets due to their young age. There were 15 patients with hypokalemia (68%) in the *SLC4A1* group, 3 (100%) in the *ATP6V1B1* group, and 2 (100%) in the *ATP6V0A4* group. A total of 24 children underwent renal Doppler ultrasound examination. Among them, 17 children (77%) in the *SLC4A1* group, 3 children (100%) in the *ATP6V1B1* group, and 2 children (100%) in the *ATP6V0A4* group had nephrocalcinois. 3 patients in the *SLC4A1* group and 1 patient in the *ATP6V1B1* group had renal malformations. One patient with *SLC4A1* mutation had hemolytic anemia. Among the three patients with *ATP6V1B1* mutation, two siblings had bilateral Mondini malformations and sensorineural hearing loss(SNHL). Among all the dRTA painets, their blood pH, blood HCO3-concentration, actual alkali excess(ABE), serum potassium decreased, serum chlorine increased, serum creatinine levels and urea nitrogen levels were normal, and urine pH could not be acidified below 5.5. The 27 children had an average disease course of 3.9 (3.9±2.7) years and an average follow-up period of 3.1 (3.1±2.3) years. 21 patients were followed up and treated regularly. After adequtate alkaline treatment ,there was an significant improvement in patients' height and weight. Metabolic acidosis, hypokalemia was recovered compared with their orignial conditions (paired t test, $P<0.05$).

Conclusion *SLC4A1* is the most common defective gene in the 27 patients with dRTA. Children with *SLC4A1* genotype have a larger age of onset, and children with *ATP6V0A4* and *ATP6V1B1* genotypes are younger. All the dRTA patients had clinical manifestations of growth retardation, hypokalemia, and nephrocalcinois. Besides, patients with *ATP6V1B1* gene mutations had early SNHL. We found no difference in the onset, clinical manifestations, severity of laboratory examinations, and prognosis among genotypes. For children with early clinical identification clues, it is recommended that early genetic sequenceing and early treatment can significantly improve the prognosis of dRTA children.

关键字 primary distal renal tubular acidosis; Genotype; Clinical phenotype; Prognosis

分类：17. Nephrology 肾脏
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Effects of TCM combined with Western medicine on CD19+ B Lymphocytes in Children with HSPN

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Abstract: Objective: In order to explore the effects of TCM treatment combined with Western medicine on blood CD19+ B lymphocytes in children with HSPN, this study retrospectively analyzed the changes in immune function of children with HSPN after TCM treatment combined with Western medicine for 6 months. Methods: A total of 46 children with HSPN were included in this study. Before TCM was prescribed for these children, urinary RBC and protein, blood CD19+ B lymphocytes and immunoglobins were tested, after TCM combined with Western medicine treatment for 6 months, such tests were done again. We analyzed the results of blood CD19+ B lymphocytes, immunoglobins according to the efficacy in children. Results: The counts of CD19+ B lymphocytes in children with complete remission was significantly reduced after TCM combined with Western medicine treatment (672.4±106.4 vs 310.9±40.2, P<0.01), the count of CD19+ B lymphocytes in partial remission or unresolved children did not change significantly after treatment (553.3±104.3 vs 345±76.48, P>0.05; 772.3±268.5 vs 407.7±55.95, P>0.05). The CD19+% in children with complete remission was significantly decreased after treatment (22.68±2.09 vs 13.47±1.09, P<0.01), and the change of CD19+% in partial remission or unresolved children was not significant after treatment (18.36±1.91 vs 16.36±2.74, P>0.05; 21.17±4.3 vs 14.07±1.48, P>0.05). Conclusion: Combination therapy with TCM and Western medicine can reduce CD19+ B lymphocytes in children with HSPN, suggesting that CD19+ B lymphocytes could be the treatment target for children with HSPN and efficacy evaluation of treatment.

关键字 HSPN; TCM combined with Western medicine; CD19+ B lymphocytes

分类：17. Nephrology 肾脏
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Clinical experience in improving the technical survival rate of early catheterization for peritoneal dialysis in children

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Objective To explore the effect of improved catheterization and various intervention methods before and after catheterization on the technical survival rate of early catheterization in children's peritoneal dialysis. Method The clinical data of 16 children with chronic renal failure treated by peritoneal dialysis from January 2016 to March 2017 in the pediatric nephrology department of our hospital were collected. All patients were treated with modified laparoscopic catheterization, preventive partial omentum resection, preoperative temporary hemodialysis, intraoperative peritoneal lavage with saline repeatedly to drainage clear, small dose of urokinase added to the dialysate routinely one week after the operation, and regular peritoneal dialysis operation training. To observe the early technical survival rate of catheterization within 3 months after peritoneal dialysis catheterization, such as poor drainage of dialysate, catheter displacement, catheter obstruction, re catheterization, and shallow polyester sheath exposure. Result 1.A total of 16 cases of surgery were collected, with an average age of 9.6 years and an average follow-up of 3 months. After these improvements, postoperative complications such as poor drainage of dialysate, catheter displacement and catheter blockage were significantly improved compared with traditional operation methods (P<0.05). There was no case of omental wrapping, no bladder injury, incisional hernia and intestinal tube injury. 2. The clinical indexes of all children were significantly improved after dialysis, and there was a significant difference compared with that before dialysis (P<0.05). Conclusion The improved catheterization of peritoneal dialysis and various intervention methods before and after catheterization can improve the early catheter technology survival rate, reduce early complications and improve the quality of life in children with long-term renal replacement therapy.

关键字 Peritoneal dialysis in children; Improved laparoscopic catheterization; Catheter technique survival rate; summarize experience

Category: 17. Nephrology 肾脏
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Posterior urethral valve in Thai boys: 30-year experience in a single center

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Abstract Content Posterior urethral valve (PUV), a congenital anomaly in boys, in the presence of a mucosal membrane causing urinary bladder outlet obstruction, is the major cause of chronic kidney disease (CKD) in boys and young males. Since the renal damage occurs in utero, urinary obstruction correction at the earliest opportunity is needed to minimize future renal damage. The objective of this study is to review the presentations, clinical course, complications, outcomes and renal survival in PUV boys.

Methods We reviewed the medical records of PUV boys treated at the Pediatric Nephrology Clinic, Prince of Songkla University, Thailand during 1991-2020.

Results The medical records of 77 PUV boys were retrospectively reviewed. The median age at diagnosis was 4.8 months (IQR 0.8-28.7). The most common presentations were urinary tract infection (UTI), poor urine steam and urine dribbling in 26 (33.8%), 19 (24.7%) and 11 (14.3%) boys, respectively.
Renal ultrasound results were available in 70 boys, of which 8 (11.4%) and 56 (80%) boys had unilateral and bilateral hydronephrosis, respectively. Of 72 voiding cystourethrogram results, 18 (25.0%) and 22 (30.6%) boys had unilateral and bilateral vesicoureteral reflux, respectively. 99mTc dimercaptosuccinic acid renal scans were performed in 30 boys; 12 (40%) and 8 (26.7%) boys had unilateral and bilateral renal damage, respectively. Fifty-nine (76.6%) boys had 149 UTIs and 42 (54.4%) boys had recurrent UTI. Forty-eight boys had valve ablation at the median age of 30.3 months (IQR 12.8-54.8)
22 boys (28.6%) developed CKD at a median age of 7.1 years (IQR 3.9-11.2). Our study identified no independent risk factors to predict CKD development.
The median age of the known survivors at the end of the study was 6.3 years (IQR 2.2-12.6); overall 5 had died, 35 survived, 18 had been returned to their original hospital and 19 had been lost to follow up. Of the 22 boys who had developed CKD, 2 had died, 8 were still alive and in our care, 8 had been returned to their original hospital and 4 had been lost to follow up. Of the 7 living had renal replacement therapy.

Conclusion In this study of 77 PUV Thai boys, UTI was the most common presentation. Recurrence of the UTI was the most common consequence and CKD was the most serious consequence. One-fourth of the boys had developed CKD at the latest follow-up.

Key words Acute kidney injury, Chronic kidney disease, Hydronephrosis, Posterior urethral valve, Urinary tract infection, Urinary tract obstruction, Vesicoureteral reflux

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分类：17. Nephrology 肾脏
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Comparative proteomic analysis of FSGS FFPE tissues from children using label-free LC-MS/MS quantitative proteomics

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Background Focal segmental glomerulosclerosis (FSGS) is the main cause of steroid resistant nephrotic syndrome (SRNS) in children. Here, we analysed FFPE protein profiles, aiming to discover disease‐specific candidates and the mechanism underlying steroid resistance in FSGS patients.**Methods** We utilized liquid chromatography tandem mass spectrometry with an Orbitrap mass analyser to quantify proteins and identify related pathways of clinically well-annotated formalin-fixed paraffin embedded (FFPE) renal biopsies of patients with steroid-sensitive (n=7) and steroid-resistant (n=11) FSGS.
Results In total, we quantified 4794 proteins were identified, of which 325 were found to be differentially expressed proteins(DEPs) between the FSGS-SR and FSGS-SS group(foldchange≥2, P＜0.05). Functional analyses of DEPs, including Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment, and protein-protein interaction (PPI) network construction, were conducted. The results revealed that the most significant up-regulated proteins were primarily related to protein transportation, regulation of the complement activation process, cytolysis and actin cytoskeleton reorganization. Meanwhile, the down-regulated proteins were primarily involved in metabolic process. Moreover, clustering analysis highlighted pathway-level (terminal pathway of complement, lysosome) differences between the FSGS-SR and FSGS-SS groups. Among these potential candidates for universal FSGS steroid resistance marker, validation analysis for LAMP1 was conducted. LAMP1 was observed to have a higher expression in glomerulus of FSGS steroid resistance.
Conclusion Our study constitutes the first FFPE tissue proteomics study for identifying proteins associated with FSGS progression and steroid resistance. These proteomic variations are potentially helpful for better predicting patient outcomes and nominating novel therapeutic targets for personalized care.

关键字 FSGS, steroid resistance, FFPE, LC-MS/MS, proteomics

分类：17. Nephrology 肾脏
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Juvenile Nephronophthisis 1 Disease: One Case Report and Literature Review

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Beckground: Juvenile nephronophthisis 1 disease is a hereditary disease characterized by renal multicysts and latent chronic renal failure, which is very rare. **Method:** Retrospectively analyzed the clinical data of a patient (female,13 years old) with juvenile nephronophthisis 1 and reviewed related literatures. Whole exome sequencing (WES) was applied to examine the DNA sample of the patient. **Results:** The case presented at the preschool stage with the symptom of microscopic hematuria. Then the main symptoms were characterized by poor appetite, anemia and chronic renal failure at the juvenile stage. Laboratory tests showed lower haemoglobin, lower specific gravity of urine and higher serum creatinine. Ultrasound showed multicysts at the corticomedullary border and medullary of the right kidney. Gene mutation analysis identified pathogenic NPHP 1 gene mutations. **Conclusions:** The clinical symptoms of Juvenile nephronophthisis 1 disease are various and sometimes not typical. By gene mutation analysis, we can reduce the possibilities of misdiagnosis and missed diagnosis and increase early diagnostic rate of the disease.

关键字 Juvenile Nephronophthisis 1 Disease; Chronic renal failure; Gene mutation analysis;

分类：17. Nephrology 肾脏
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The predicting value of urinary epidermal growth factor in pediatric IgA nephropathy

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Background　Pediatric IgA nephropathy(IgAN) is one of the most common glomerular diseases, with 20% of patients progressing to end-stage renal disease within 25 to 30 years. Predicting value of urinary epidermal growth factor(uEGF) has been validated in diabetic nephropathy, Alport syndrome and some other kidney diseases. However, its predictive ability in pediatric IgAN is still unknown.
Methods　Pediatric IgAN enrolled in Registry of Pediatric IgA Nephropathy in Chinese Children (RACC), at our center from Jan. 2016 to Mar. 2019, were included. Urine samples at biopsy have been stored at -80/-20 ℃. Urinary EGF was measured in duplicates using ELISA (R&D) and normalized by urine creatinine (uEGF/uCr). According to uEGF/uCr, patients were divided into low uEGF group and normal uEGF group. Complete proteinuria remission was defined as 24-hour urinary protein ≤150 mg/day or urinary protein/creatinine ≤ 0.2mg/mg.
Results　Thirty-eight boys and sixteen girls were included for analyses, at a mean age of 10.5 years. At biopsy, average eGFR was 102.1 ± 34.9 ml/min/1.73 m2, and 24-hour urinary protein was 46.3 (10.8, 71.2) mg/kg. uEGF/uCr was lower in IgAN children, compared with healthy controls. At baseline, uEGF/uCr was positively correlated with eGFR (r=0.745，P<0.001, adjusted by age). No correlation was found between uEGF/uCr and urinary protein (P > 0.05). During follow-up, low uEGF group had lower rate of complete proteinuria remission, compared with normal group (65.4% vs 80.0%). However, no significant difference was found.
Conclusion Decreased uEGF/uCr at biopsy might be associated with lower rate of proteinuria remission in our study. Further study with larger sample size and longer follow-up is necessary to confirm the predicting role of uEGF, as a biomarker of pediatric IgAN

关键字 IgA nephropathy, children, urinary epidermal growth factor

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Higher urine exosomal miR-193a is associated with a higher probability of primary focal segmental glomerulosclerosis and an increased risk of poor prognosis among children with nephrotic syndrome

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Abstract
Background: In children, focal segmental glomerulosclerosis (FSGS) is one of the most common primary glomerular diseases leading to end-stage renal disease. Exosomes facilitate communication between cells by transporting proteins and microRNAs. We aimed to investigate the utility of urine exosomal miR-193a for diagnosis and prognosis estimation among patients with primary FSGS, and preliminarily explore the regulation mechanism of exosome secretion from podocytes.
Methods: Specimens of urine were obtained from patients with primary FSGS, minimal change nephropathy (MCN) and IgA nephropathy (IgAN), followed by exosome isolation. We quantified urine exosomal miR-193a based on quantitative reverse transcription-polymerase chain reaction, and evaluated its applicability using area-under-receiver-operating-characteristics curves (AUROCs). The semiquantitative glomerulosclerosis index (GSI) was used to evaluate the degree of glomerulosclerosis according to the method of Raij etal. We further used FAM-labeled miR-193a-5p to examine exosome shuttling using confocal microscopy for visualization, and explored the regulation mechanism of exosomes release from podocytes using Fluo-3AM dye.
Results: Urine exosomal miR-193a levels were significantly higher in patients with primary FSGS than those with MCN and IgAN. The AUROCs for discriminating between primary FSGS and MCN or IgAN were 0.85 and 0.821, respectively. Urine exosomal miR-193a levels positively correlated with GSI in patients with primary FSGS. We further found that kidney tissues from these patients had increased CD63 expression involving podocytes in non-sclerotic tufts. Exosomes from cultured podocytes could transport miR-193a-5p to recipient cells, potentially through a calcium-dependent release mechanism.
Conclusion: Urine exosomal miR-193a might be harnessed as a non-invasive marker for diagnosis and outcome assessment among patients with primary FSGS. Exosomes were potential vehicles for miRNAs shuttling between podocytes, and released from podocytes in a calcium-dependent manner.

关键字 exosome, microRNA-193a, focal segmental glomerulosclerosis, nephrotic syndrome

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EFFECTIVENESS OF VITAMIN A SUPPLEMENTATION ON RENAL SCARRING AMONG INFANTS AND CHILDREN POST-ACUTE PYELONEPHRITIS INFECTION: A META-ANALYSIS

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Abstract Content Background: Renal scarring is a consequence of acute pyelonephritis in infants and children and is detected by DMSA renal scan. Studies have shown the protective effect of Vitamin A supplementation in mitigating the development of renal scarring through regeneration and restoration of epithelial mucosal surface. Hence, vitamin A supplementation has the potential to prevent the formation of renal scars post-acute pyelonephritis infection.

Methods Design: This study is a meta-analysis.

Patient/Participants: The population of interest was infants and children aged 1 month to 18 years who had acute pyelonephritis. In the 4 included studies, there were 128 respondents in the Vitamin A supplementation group and 142 in the control group, with a total of 270 samples.

Data Sources: Researches were searched at Cochrane Library, PubMed Central, PubMed.gov, EBSCO Host, ScienceDirect, Google Scholar, Wiley Online, and ProQuest.

Intervention: This study included Randomized Control Trials (RCTs) comparing vitamin A supplementation plus antibiotic with a placebo plus antibiotic among infants and children post-acute pyelonephritis. The intervention will be Vitamin A supplementation given for 1-10 days.

Main Outcome Measures: The proportion of abnormal renal scan results were extracted and recorded. Odds ratio was used as the effect measures and was estimated using Review Manager. The primary outcome is the proportion of participants who had normal DMSA scintigraphy renal scan result after 3-6 months follow-up.

Results Results: The likelihood of renal scarring was significantly lower in the Vitamin A supplementation (OR=7.13, p=0.0001). Results also showed that there was no evidence of any heterogeneity among the included studies ($\chi 2$=0.86, p=0.83, I2=0%; $\tau 2$=0.00).

Conclusion Conclusion: Vitamin A supplementation is a cost-effective and readily available form of anti-oxidant therapy which can reduce renal scarring post-acute pyelonephritis infection among children.

Key words Keywords: Acute Pyelonephritis; Meta-Analysis; Renal Scarring; Vitamin A Supplementation

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preventing renal scarring after acute pyelonephritis. Iranian Journal of Kidney Diseases, 5(5) 320 - 323.

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Tubulointerstitial Nephritis and Uveitis Syndrome Progressing to Chronic Kidney Disease in Children

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Tubulointerstitial nephritis and uveitis (TINU) syndrome is a rare disease in children, with the probability of progressing to chronic kidney disease (CKD), even resulting in irreversible renal dysfunction. A total of 5 patients were enrolled, and followed up for more than 12 months. All of five patients suffered from acute kidney injury (AKI) at diagnosis, with the median glomerular renal filtration (GFR) value 69.7ml/min•1.73m2. The renal histology for each patient was characterized by the interstitial infiltration of inflammatory cells, and focal tubular atrophy revealed in three patients. Oral prednisone was administered for more than 6 months. During the follow-up, four children progressed to CKD, despite all the patients had an improvement of renal function. In our article, we found the gender, presence of focal tubular atrophy, the time between the initial symptoms and treatment were likely to be the risk factors for development of CKD.

关键字 Tubulointerstitial nephritis and uveitis syndrome; Pathological feature; Chronic kidney disease; Children; Prognosis

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Henoch-Schonlein purpura nephritis complicated with reversible posterior leukoencephalopathy in children: a case report and literature review

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[Abstract]Objective:To explore the clinical characteristics of children with Henoch-Schonlein purpura nephritis complicated with reversible posterior leukoencephalopathy. Case report: In this article, we reported a case with hemorrhagic rash in both lower limbs, black stool and microscopic hematuria. Consider purpura nephritis, take hormone regularly, recheck urine routine is normal, and gradually reduce hormone until stopping medication. One year after stopping the drug, the child appeared proteinuria and hematuria again, and the urine routine showed pathological tubular type.Renal biopsy revealed focal proliferative purpura nephritis, ISKD, type IIIA. After three times of plasma exchange, two times of hemodialysis and the first course of methylprednisolone pulse therapy, the child developed convulsions, and the measured blood pressure increased to 143/80mmHg. The possibility of reversible posterior leukoencephalopathy was in head MRI.After amlodipine, sodium nitroprusside and phentolamine, blood pressure returned to normal and clinical symptoms improved. Conclusion: In children with Henoch-Schonlein purpura nephritis complicated with reversible posterior leukoencephalopathy, the manifestation of hypertension may not be obvious, but the manifestation of central nervous system is obvious, and brain injury may also occur at normal high blood pressure. Early detection and early treatment are needed for these children.

关键字 [Key words] Children, Henoch-Schonlein purpura nephritis, reversible posterior leukoencephalopathy, case report.

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Integrative analysis of gut microbiota and fecal metabolites in rats after prednisone treatment

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Background
Prednisone (PRED) is a synthetic glucocorticoid (GC) widely used in immune-mediated diseases for its immunosuppressive and anti-inflammatory properties. The effects of GC are achieved by genomic and non-genomic mechanisms. However, non-genomic effects are largely unknown. Thus, we aimed to investigate how long-term prednisone therapy changed the composition of gut microbiota and fecal metabolites in rats.
Methods
Male Sprague-Dawley rats were randomly assigned to control (CON) and prednisone (PRED) group which received prednisone treatment daily for 6 weeks by gavage.V3-V4 regions of bacteria 16S rRNA gene were amplified and sequenced after total bacteria DNA was extracted from fecal samples. The qualified reads were clustered into operational taxonomic units (OTUs) by UPARSE pipeline. Alpha diversities including Chao1, ACE, Shannon, Simpson and coverage index were calculated by using Mothur software. R Project was used in Principal Coordinate Analysis (PCoA) including Bray-Curtis distance, Jaccard, unweighted and weighted UniFrac metric. Compositional alteration of gut microbiota at taxonomic levels was analyzed by using Metastats method. Meanwhile, fecal metabolites were quantitated in an ultra-performance liquid chromatography.
Results
Similar microbial richness and diversity between CON and PRED groups were indicated by the results of alpha diversity. Gut microbial community differed significantly between two groups. The relative abundance of genera Eisenbergiella, Alistipes and Clostridium XIVb decreased, whereas Anaerobacterium augmented significantly in rats after 6-week prednisone treatment. Totally 11 downregulated and 10 upregulated fecal metabolites were identified. Differential fecal metabolites were enriched in the pathways including phenylalanine metabolism, butanoate metabolism and propanoate metabolism. The lower production of short chain fatty acids were associated with the decreased relative abundance of genera Alistipes, Clostridium XIVb and increased Anaerobacterium.
Conclusions
The composition of gut microbiota and fecal metabolites were changed after long-term prednisone treatment. It may help to understand the pharmacology of prednisone.

关键字 Prednisone, Gut microbiota, Metabolite, Rat

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A predictive system for Henoch-Schönlein purpura nephritis established by multivariate analysis plus nomogram model in Chinese hospitalized children

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A predictive system for Henoch-Schönlein purpura nephritis established by multivariate analysis plus nomogram model in Chinese hospitalized children

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Background
Henoch-Schönlein purpura (HSP), also named as IgA vasculitis, usually affects the small vessels in skin and multiple internal organs, and accounts for over half of the primary vasculitis diagnosed in childhood. It mainly manifests as non-thrombocytopenic purpura, arthritis/arthralgia, abdominal pain, gastrointestinal bleeding and renal involvement. Generally speaking, HSP is a self-limited disease that initially lasts an average duration of 4 weeks, whereas it also becomes an indication for emergency hospitalization once severe systemic inflammation persists or renal involvement is involved. As we all know, the long-term prognosis of HSP is largely dependent on renal involvement. Currently, a number of investigators have attempted to find out the possible risk factors for predicting HSP nephritis (HSPN). The present study aimed to identify the risk factors of HSPN and establish a new scoring system for predicting renal involvement in HSP patients.

Methods
A total of 1655 Chinese children with HSP were recruited from January 2015 to December 2020. The demographic features, clinical manifestations, laboratory findings and patients' histories associated with HSPN onset were retrospectively assessed. Independent risk factors were confirmed by multivariate analysis and then assembled into a nomogram for predicting HSPN.

Results
A total of 1655 patients with HSP, younger than 17 years old, were enrolled in the present study, including 945 (57.10%) boys and 710 (42.90%) girls from January 2015 to December 2020 (male: female = 1.3:1). The total number of hospitalization was 2313 during the observational period, and 301 HSP patients were hospitalized more than one time. The average age was 7.92 ± 2.98 years old and median age was 8.00 years old. Interquartile range (IQR) for the onset age fell in the interval between 6 and 10 years old. The estimated annual incidence of HSP was 7.61 - 9.01 per 100,000.

The demographic, clinical and laboratory characteristics of HSP patients with and without renal involvement were analyzed by univariate and multivariate analysis. The following variables: age >7.5 years, relapse, severe abdominal symptoms, intervals from symptoms onset to diagnosis more than 6 days, persistent purpura more than 12 days and C3 less than 0.225 g/L were confirmed as the independent risk factors for HSPN by multivariate analysis. Considering the low OR value (0.223) and poor discrimination ability (AUC of 0.417), C3 was excluded from the establishment of predicting model. Based on the results of logistic regression analysis, a nomogram model was developed. The total points (0-100) accumulated by each variable' score corresponded to the predicted probability of HSPN. Patients with relapse were given 27.5 points, whereas patients without relapse got 0 point; patients with presence of severe abdominal pain were given 17.0 points, whereas patients without severe abdominal pain got 0 point; and according to the specific values of age, interval from symptom onset to diagnosis and duration of purpura, patients would be given 0 - 21 points, 0 - 59 points and 0 - 100 points, respectively. The calibration curves of the nomogram demonstrated good correspondence between predicted outcome and actual outcome of HSPN in this nomogram model.

Conclusions

Interval from symptom onset to diagnosis is a unique predictor of HSPN in the present study. The predicting model for HSPN is established with an excellent discrimination accuracy.

关键字 Henoch-Schönlein purpura; Multivariate analysis; Nephritis; Nomogram; Risk

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AlteringTh17/Tregbalancethroughgalectin-9andTim-3alleviatesdamageinrenalIRImice

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Abstract
Thecoreofpathophysiologicalmechanismofrenalischemicreperfusioninjury(IRI)istheoutofcontrolofinflammatoryresponse,inwhichtheearlyandlateCD4+Tcell-mediatedimmuneinflammationplaysanimportantrole.Therefore,controllingtheinflammatoryresponsecanreducerenalinjuryandpromotetherepairofrenalinjury.StudieshaveshownthatTh17cellsarethepathogenicCD4+TcellsubtypeinAKI,whileFoxp3+regulatoryTcells(Tregs)haveprotectiveeffects.Galectin-9(Gal-9)isoneoftheligandsofTcellimmunoglobulinandmucopolysaccharidemolecule-3(Tim-3).Tim-3andGal-9caninteracttoprovidenegativecostimulatorysignalforCD4+Tcells,inhibitimmuneresponse,induceapoptosisofTh17cellsandpromotetheproliferationofFoxp3+Tregs.WehypothesizedthatTim-3andGal-9mayregulatethedevelopmentofTh17/TregcellsafterrenalIRIandmaybetherapeutic.Recombinantadenovirus-gal-9(rAAV9)wasinjectedintothemicebytailvein2weeksbeforerenalIRI.Theresultsshowedthatoverexpressionof Gal-9canreducetheproportionofTh17cellsandthelevelofpro-inflammatorycytokinesinthekidney,increasetheratioofFoxp3+TregsandIL-10expression,reducethepathologicaldamageofthekidneyandthemortalityofbilateralrenalIRImice.Tim-3monoclonalantibodycaninducetheexpressionof Th17cellsintheearlystageofrenalIRIandsignificantlydownregulateFoxp3+Tregsinthelatestageofrenal IRI,whichindicatesthatTim-3andGal-9areinvolvedintheprocessofrenalIRIandcanchangethebalanceofactivatedCD4+Tcellsubsets,whichmaybecomeapotentialnewimmunotherapytargetinrenalIRI.
Keywords:Galectin-9.T-cellIgmucin3.Th17.Treg.Kidney

关键字 Galectin-9.T-cellIgmucin3.Th17.Treg.Kidney

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Hypertension Crisis As The First Symptom Of Renovascular Hypertension In Children: A Retrospective Study From A Single Center In China

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Renovascular hypertension (RVH) is caused by stenosis of the main or branch of the renal artery. It is an important cause of secondary hypertension and one of the main causes of hypertensive crisis (HTN-C).The objective of this study is to describe the characteristics of RVH with or without HTN-C in children aiming to improve patients' management.Here, we retrospectively analyzed the data of 2746 inpatient children (0-18 years old) with hypertension treated at the First Affiliated Hospital, Sun Yat-Sen University from January 1991 to February 2019. Of them, 57 children with RVH were eligible for this study, and comprised of 75.4% (43/57) boys and 24.6% (14/57) girls. 84.2% of the RVH cases were ≥6 years old. The average time from the first onset of symptoms of hypertension to hospital admission was 0.3 (0.0-4.4) months. There were 4 (7.0%) cases in the non-hypertensive crisis group and 53 (93.0%) in the HTN-C group. Also, 20 cases were in the hypertensive urgency (HTN-U) group and 33 in the hypertensive emergency (HTN-E) group. Systolic Blood Pressure (SBP) , Diastolic Blood Pressure (DBP) and the onset of symptoms were significantly different between HTN-U and HTN-E groups. Patients from the HTN-U group were mainly asymptomatic (45.0%, 9/20) while those from the HTN-E group mainly presented with neurological symptoms (72.7%, 24/33). The number of patients with unknown causes was 32 (56.1%). The top three known etiologies of RAS were TA (44.0%, 11/25), congenital renal dysplasia (24.0%, 6/25) and fibromuscular dysplasia (12.0%, 3/25). As for the target organ damage of RVH, 11/50 (22.0%) cases were diagnosed with TA, 5/50 (10.0%) with congenital renal dysplasia, 3/50 (6.0%) with fibromuscular dysplasia, and 28/50 (60.0%) were unknown causes. Patients with RVH had a higher prevalence of left ventricular hypertrophy (68.6%, 35/51) , retinopathy (75.0%, 21/28), hypertensive encephalopathy (37.7%, 20/53), proteinuria (36.8%, 21/57). Our findings suggest that children with HTN-C as the first symptoms, especially for males over 6 years old, should be assessed for RVH even if they have no overt clinical manifestations. When other systemic symptoms such as the nervous system appear, the extent of target organ damage should be evaluated. As preventive measures, the population's awareness regarding hazards of hypertension should be increased and routine monitoring of blood pressure during children's physical examinations is advised.

关键字 Renovascular hypertension, children, Hypertensive crisis, hypertensive urgency, hypertensive emergency

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Alleviation of lupus nephritis by IL-35 regulated JAK/STAT signaling pathway in mesangial cells

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Objective: In this study, we have investigated the potential regulatory mechanisms of IL-35 in alleviating lupus nephritis (LN) by regulating JAK/STAT signaling pathway in mesangial cells.

Methods: Urinary differential proteins between juvenile systemic lupus erythematic (JSLE) patients with nephritis and normal control were found by proteomics assay. Co-immunoprecipitation (Co-IP) combined with mass spectrometry (MS) were verified the interactive proteins as above found. Bioinformatics analysis including Go ontology (GO), KEGG and String proposed IL-35 regulatory signaling pathway. The pathway was proved by RNA-sequencing and flow cytometry assays in mesangial cells. Then, the treatment effect of nephritis was confirmed via overexpression of IL-35 and transplantation of regulatory T cells (Tregs) in lupus mice model. Finally, the inflammatory cytokines and Janus kinase (JAK)/ signal transducer and activator of transcription (STAT) signaling pathway were justified through IL-35 treated lupus mice with nephritis.

Results: We have identified 105 significant differentially expressed proteins (DEPs) between JSLE-LN patients and normal controls. When combined DEPs among groups, we found LAIR1, PDGFRβ, VTN, EPHB4 and EPHA4were down regulated in JSLE-LN. Moreover, they have an interactive network with PTPN11 and FN1, which were also involved in IL-35 related JAK/STAT signaling pathway. Interestingly, LAIR1 was significantly correlated with SLEDAI, %CD19+ B and %CD3+ T cells in JSLE-LN. Through bioinformatics analysis of Co-IP with MS results, including GO, KEGG and String, LAIR1 interactive protein expression genes like Sfxn3, Ptpn23, Ddx21, Ehd1, Tubg1 were upregulated by IL-35, while Myh10 was downregulated. Therefore, we presumed a signal network among these interactive proteins, JAK/STAT and IL-35. Meanwhile, the downregulated phosphorylated STAT3 and upregulated phosphorylated JAK2 and STAT1 in IL-35 overexpressed mesangial cells, as well as the heat map of presumed signal network were confirmed the potential regulatory mechanisms of IL-35 in alleviating LN. Furthermore, a remission of histopathological characteristics of nephritis including urine protein and leukocyte scores was observed in IL-35 overexpression plasmid and transferred Tregs treated lupus mice. Meanwhile, there were phosphorylated activation of IL-35 related JAK/STAT and MAPK signals, and significant upregulation of Tregs in spleen, thymus and peripheral blood. Moreover, the significant decreased CD90+αSMA+ mesangial cells and a decreased pro-inflammatory cytokines like IL-6, IL-12, IL-1β, TNF-α and IL-17A, while a significant increment of IL-10, TGF-β1 and IFN-γ were found in IL-35 and Tregs treated groups, when compared with PBS and IL-35 null vector treatments.

Conclusion: Our study provided a reference proteomic biomarker map for JSLE-LN, and elucidated a proof that IL-35 may interact with PTPN11-JAK-STAT-FN1 to affect

JAK/STAT and MAPK signaling pathways in alleviating inflammation in JSLE-LN. This finding may provide a further prospective mechanism for JSLE-LN clinical treatment.

关键字 IL-35, LAIR1, JAK/STAT, lupus nephritis

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A case of Schimke immune bone dysplasia caused by SMARCAL1 gene complex heterozygous mutation began with focal segmental glomerulosclerosis

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Abstract: Objective To analyze the clinical characteristics, genotype and prognosis of Schimke immune bone dysplasia (MIM242900). **Methods** The clinical data of a child with Schimke immune bone dysplasia were analyzed retrospectively and the literature was reviewed. **Results** The case was a girl who underwent cesarean section at 36^{+3} pregnancy because of "slow fetal growth". Her birth weight was 2.02kg, body length was 45cm, and her parents were not close relatives. At the age of 3 years old and 10 months, she was hospitalized due to poor growth and development. The physical examination showed that the height was 83cm, the body weight was 13.8kg, the head circumference was 48cm, the chest circumference was 51cm, the abdominal circumference was 52cm, the sitting height was 42cm, the physical development was backward, the intelligence was normal, and a milk coffee spot could be seen in the abdomen with a diameter of 3mm×3mm, several moles can be seen in the armpit, double eyelids are swollen, the neck is short, the bridge of the nose is collapsed and the abdomen is prominent. The clinical manifestations were recurrent infection, convulsions (right focal). Laboratory examination showed nephrotic proteinuria, hypoalbuminemia, hypercholesterolemia, decreased thyroid function and decreased T lymphocyte count. Cranial MRI showed multiple flake high signal shadows in the left temporal parietal occipital cortex, left hippocampus and left thalamus on T2WI, DWI and flair sequences, and flake low signal shadows in the left semi oval center on DWI sequences. After glucocorticoid treatment, it showed hormone resistance. Renal biopsy showed focal segmental glomerulosclerosis (FSGS) (NOS type). Gene sequencing showed a compound heterozygous mutation of *SMARCAL1* gene (1 pathogenic mutation, 1 suspected pathogenic mutation and 1 unknown mutation). Both parents had a heterozygous mutation of *SMARCAL1* gene, which was consistent with autosomal recessive inheritance. The patients were treated with glucocorticoid and mycophenolate mofetil orally. She was followed up to 4 years old and 1 month, here was no renal function damage, no repeated infection, but there was still nephrotic proteinuria. **Conclusion** The pathological type of nephrotic syndrome with hormone resistance should be determined as soon as possible, and the genetic background of children with FSGS should be determined. Schimke immune bone dysplasia is a rare disease with poor prognosis. Children with multisystem damage should actively carry out gene testing, which can provide great help for definite diagnosis, guide treatment, and correctly evaluate the long-term prognosis.

关键字 SMARCAL1; Schimke immune bone dysplasia; Nephrotic syndrome; focal segmental glomerulosclerosis

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A case report of ESRD renal failure caused by TRPC6 gene splicing mutation

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Background： Canonical transient receptor potential channels (TRPCs) are nonselective, high calcium permeability cationic channels. The TRPCs family includes TRPC1-7. These channels are widely expressed in the cardiovascular and nervous systems and exist in many other human tissues and cell types, playing several crucial roles in the human physiological and pathological processes. Mutations in the TRPC6 gene lead to focal segmental glomerulosclerosis type 2 (OMIM:603965), an autosomal dominant genetic disorder. It is characterized by segmental glomerular sclerosis, proteinuria, low glomerular filtration rate, and progressive decline in renal function, often progressing to end-stage renal disease (ESRD), requiring dialysis or kidney transplantation in severe cases.
Method： A girl undergoing peritoneal dialysis with rapid progression to ESRD due to TRPC6 gene mutation is reported in this paper.1.Clinical data: gender, age, medical history, clinical manifestations, and other general information of the children were collected; Serum albumin, cholesterol, serum creatinine, urinary protein, and other laboratory test indicators; Genetic test results and follow-up. 2. Minigene In vitro test: We constructed the sequencing maps of wild-type(WT) and TRPC6 mutant(TRPC6-mut) Minigene, and inserted them into two different vectors, respectively. Then we transfected the recombinant vector into two different cell lines 293T and Hela. After 48h, we collected the 8 samples, and performed RT-PCR transcriptional analysis and shear band sequencing, respectively.
Results： The proband was a 13-year-old girl, and was hospitalized for ″bilateral lower limb edema for 1 day without obvious cause″.On admission, her proteinuria was 3+, hematuria was 3+, serum creatinine was 1172umol/L, serum urea nitrogen was 24.73mmol/L, and serum uric acid was 433umol/L.One day later, she developed nausea, vomiting, palpitation, and other symptoms. To clarify the cause, she was transferred to our hospital. The whole exon gene was performed and mutations of COL4A4 gene TRPC6 gene and CUBN gene were found. According to the clinical symptoms, we believed that the mutation of the TRPC6 gene was the cause of her acute renal failure. The mutation type was NM_004621.5: c.2645-1G>A, that is, the first base downstream of 2645 changed from G to A. In Minigene，RT-PCR transcriptional analysis and shear band sequencing results of two different vectors showed that compared with the WT, the left side of the Exon13 of TRPC6-mut was missing 1bp base, which was a shear mutation.c.2645-1G>A can affect the normal splicing of mRNA.
Conclusions： Among the previously reported cases, TRPC6 gene mutations were mostly missense mutations, and a few were splicing mutations. Here, we reported a case of a child with the rapid progression to ESRD due to TRPC6 splicing mutations, which was verified in vitro. Our case broadens the gene spectrum of TRPC6, which has certain significance for early identification and diagnosis.

关键字 TRPC6;gene mutation;Minigene;ESRD;renal failure

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Analysis of clinical phenotype, genotype, and pathological phenotype of LAMB2 mutation

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Background: LAMB2 mutations can lead to congenital nephrotic syndrome with ocular abnormalities or isolated kidney disease. The renal pathology is mostly Diffuse Mesangial Sclerosis (DMS) and Focal Segmental Glomerulosclerosis (FSGS). Clinical phenotype characteristics of LAMB2 mutations are reported here.
Method: The clinical phenotypic and genotypic characteristics of children with isolated renal lesions caused by LAMB2 mutation were retrospectively analyzed from 2013 to 2019. Meanwhile, PubMed, Medline, and Wanfang databases were retrieved to analyze and summarize the clinical phenotypic, pathological, and genotypic characteristics of the patients with LAMB2 mutation.
Results:1.There were 2 cases of Steroid-resistant nephrotic syndrome caused by LAMB2 mutation in our center,1 case of basal membrane lesion, and 1 case of FSGS. LAMB2 mutations are Exon32c.5390G>T(p.Cys1797Phe),Exon19c.2557C>T(p.Arg853*) and Exon27c.4370G>A(p.R1457Q),Exon23c.3325G>A(p.E1109K) respectively. 2. About 37 children with LAMB2 mutations were retrieved, including 24 patients with renal biopsy in the literature. 13 cases of FSGS,4 cases of Minimal Change Disease (MCD), 1 case of DMS, 1 case of IgM nephropathy,2 cases of the thin basement membrane, and 3 cases of mesangial hyperplasia were found. Among them, 8 cases had basement membrane tear. 11 cases were homozygous,22 cases were complex heterozygosity, and 4 cases were heterozygous mutation. The clinical phenotype was congenital nephrotic syndrome or Steroid-resistant nephrotic syndrome.
Conclusions:1.LAMB2 mutations may cause delamination tear of glomerular basement membrane. 2. The extrarenal manifestations caused by LAMB2 mutations are mostly various ocular abnormalities, as well as respiratory,digestive and nervous system abnormalities.3. The children who did not progress to ESRD during adolescence had no extrabrenal manifestations.

关键字 Pierson syndrome; lesions in the basement membrane; Steroid-resistant nephrotic syndrome; LAMB2 mutation

分类：17. Nephrology 肾脏
1761

Clinical and Hereditary Disease Analysis of Children and Adolescents with End-stage Renal Disease in a Single-Center

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Objective
This study aimed to investigate the etiological composition, clinical features, renal biopsy pathology, clinical treatment, prognosis and prognosis of children with ESRD. To summarize the clinical characteristics of the progression of children with CKD to ESRD. So as to provide reference for the diagnosis and treatment of hereditary related CKD children,we analyzed the characteristics of clinical phenotype and genotype of children with ESRD.
Methods
29 clinical cases of ESRD were summarized from January 2010 to December 2019 in Puyang Oilfield General Hospital affiliated to Xinxiang Medical College.We have analyzed the results of whole exome sequencing (WES) on 14 children with ESRD.
Results
The age of first diagnosis of 29 patients with ESRD ranged from 0.6 to 16 years old. The disease progressed to ESRD ranged from 1.4~19.9 years. The pathogenesis of ESRD included steroid-resistant nephrotic syndrome (8 cases), chronic glomerulonephritis (6 cases), Alport syndrome (4 cases), congenital anomalies of the kidney and urinary tract (2 cases), lupus erythematosus nephritis (1 cases), unknown etiology(1 cases). The rate of renal biopsies was 37.9%. Among them, the most common renal biopsies were FSGS (6 case), HSPN(1 case), MCD(1 case), MSPGN(1 case), AMN(1 case), SLEN(1 case). WES were performed in 16 cases of ESRD. 11 different pathogenic genes were detected in 12 cases, the positive rate was 75%. In 12 cases of ESRD, one case diagnosed as AS was attributed to mutation in COL4A5. Four cases were early diagnosed unknown etiology, through WES found pathogenic genes: WT1, ANKS6, NPHP1, COL4A5. Four cases with SRNS were attributed to mutation in NPHS1, TRPC6, PAX2, COL4A3. Two mutations in ADCK4, LMX1B were detected in two cases with CGN. One case was diagnosed as cystic nephropathy with the pathogenic gene: PKHD1. Three children were clinically diagnosed SRNS, one child was diagnosed as cystic kidney disease,but we didn,t detect any pathogenic gene.
Conclusions
SRNS was the main cause of ESRD in children and adolescents in this study. We found the majority of children with ESRD before 18 years old were caused by single gene mutation.

关键字 Whole exon gene sequencing; Chronic kidney disease; Rnd-stage renal disease

分类：17. Nephrology 肾脏
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One child with homozygous variation of ADCK4 gene presented with renal tubule interstitial damage in purpura nephritis

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Backgrounds:To investigate the relationship between ADCK4 gene variation and chronic kidney disease in children.
Methods: Whole exon sequencing was used to analyze the relationship between gene variation and clinical manifestations in a child with purpura nephritis progressing to end-stage renal disease in our hospital by collected the general condition, laboratory examinations and renal pathology results of the children.
Results：This male child with skin purpura had no obvious cause at the age of 13. After 1 week of treatment, the rash disappeared,but urine protein: +, he was hospitalized as "Purpura nephritis", and was given oral treatment of "Prednisone 40mg/d", and no rash occurred again. 2 months later urine routine appeared:urine protein ++. Urine routine tests: Elevated 24-hour urinary protein excretion (UPE) (1842.7mg/d), α-1 microglobulin >19.09mg/L, urine β2 microglobulin 227.57μg/L. Re-examination of urine routine showed protein 2+~3+, Urinary occult blood -, and Urine glucose -. Serum chemistry: Total protein 61.3g/L, Alb 37.8g/L, Serum creatinine 65.3μmol/L, Urea：5.76mmol/L, Total cholesterol:8.08mmol/L, complement C3, C4, IgA , IgM and the total CoQ10 contents in blood were all at normal levels; no obvious abnormality in urinary system ultrasound,Though taked oral prednisone and add Mycophenol ester acid regularly,urinary protein did not decrease after treatment. Renal pathology: There were 9 glomerulus in renal puncture tissue, one of them was segmental sclerotic glomerulus, the rest of the pathologies of renal biopsy were mild mesangial hypertrophic glomerular lesions, PAS staining reveals retraction and collapse of the renal tubular, with renal tubular epithelial vacuolation and granular degeneration.The epithelial cells of the renal tubules were focal atrophy, and protein tubules can be seen in the lumen of the renal tubules.Renal interstitial focal lymphocyte infiltration with fibrosis, arteriole wall thickening. Immunofluorescence: numerous irregularly shaped mitochondria with deranged cristae in glomerulus and tubules were identifified.Segmental effacement of foot processes were present.The formation of a cellular crescent in the renal follicle, epithelial lysosomes increased in renal tubules.Immunofluorescence was for IgG：+-, IgM：++, IgA：+++, C3：+++, C1q：-. Electron microscopy: Pathology of renal biopsy was mild mesangial hypertrophic glomerular lesions, and there were electronic_x0002_dense deposits. Examination revealed mitochondrial normalities. Alteration of protein expression of ADCK4 in nephridial tissue was not detected in immunohistochemistry. Pathological diagnosis: mild mesangial hyperplastic purpura nephritis (type ii B) , with renal tubule injuried. After 3 years, he was diagnosied as end-stage renal disease and began hemodialysis treatment. Genetic analysis was perfermed and A homozygous variation of C. 737G>A (P.S246N) in exon 9 of ADCK4 gene in this child, whose healthy parents were heterozygous carriers. According to relevant literature and database, the C. 737G>A mutation is the reported ADCK4 gene mutation, which is considered to be A hot spot mutation in Chinese Han population.
Conclusions:We studied a child with purpura kidney whose renal pathology was mild mesangial hyperplastic purpura nephritis (type ii B) with tubular interstitial damage.

IgA deposition was observed by immunofluorescence and was not responsive to hormone and immunosuppressive therapy. More than 3 years after the onset of ESRD, the whole exon gene sequencing showed the reported pathogenic variation of ADCK4 gene, but the blood coenzyme Q10 was normal. Electron microscopy examination revealed mitochondrial normalities in this case, in podocytes as well as in renal tubular epithelial cellls. Alteration of protein expression of ADCK4 in nephridial tissue is not detected. The relationship between kidney disease and ADCK4 gene variation in this child needs further study.

关键字 ADCK4;gene;ESRD

分类：17. Nephrology 肾脏
1787

Clinical analysis of 30 children by gene diagnosis of Alport syndrome

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Abstract Objective: to investigate the clinical significance of the clinical phenotype and gene mutation detection in children with Alport syndrome.

Method: the data of 30 children with gene mutation admitted to Guangzhou No.1 People's Hospital from January 2013 to June 2017 were retrospectively analyzed. Collecting of peripheral blood samples from children and their family members .Then using gene sequencing exon sequence capture technology to find out whether there is mutation gene including IV type collagen alpha 3 chain (COL4A3), alpha 4 chain (COL4A4) or alpha 5 chain (COL4A5).And gene mutations of related family members were identified by Sanger method.

Result: 30 children with AS were diagnosed by gene detection. Renal biosy was performed in 18 cases of 30 children with AS,and the results of light microscopy were varied. Electron microscopic examination revealed diffuse thinning, thickening and delamination of the glomerular basement membrane (GBM) in 5 cases(16.67%). The electron microscopic examination shows thin basement membrane disease in 4 cases(13.33%). 3 cases (10.00%) of immunofluorescence shows type IV collagen alpha 3, alpha 5 chain negative in renal tissue. 22 cases were diagnosed X linkage dominant hereditary Alport syndrome (XL-AS) by gene text,finding 8 new mutation sites of COL4A5. Genetic diagnosis of 8 children with autosomal recessive inheritance, and 3 new COL4A4 mutations were found.

Conclusion: The clinical manifestations of children with Alport syndrome are diverse, lack of specificity, and the pathological types of renal tissue are different. It is difficult to diagnose early. Gene detection contributes to the early diagnosis of AS, to judge the prognosis of the children, and to avoid unnecessary drug treatment.

关键字 Alport syndrome ; gene diagnosis; type IV collagen; children

Ultrasound Radiology

影像

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A case of fibrofatty hamartoma in the entire spinal canal of a child

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Abstract
Fibrofatty hamartoma is a rare benign lesion, which involves more peripheral nerves, and even less common central nervous system. To our knowledge,there are no reports of fibrofatty hamartomas involving the central nervous system (up to the fourth ventricle and down to the entire spine).We reported a case of an 8-month-old child who went to see a doctor due to unstable sitting and deflection. After two intracranial and spinal operations, the final pathological diagnosis was fibrofatty hamartoma and the postoperative recovery was good. We describe the MRI findings of the lesion, which can characteristically show the fat, and fibrous tissue within the lesion. The lesion involves the fourth ventricle and the entire spine.

Introduction
Fibrofatty hamartoma is a rare disease that involves more peripheral nerves[1], most commonly in the upper limbs. It is characterized by excessive growth of fat and fibrous tissue in the nerve, resulting in neurological compression and corresponding clinical symptoms. MRI reports are most often reported as a fatty hamartoma of the median nerve, and the age is less than 30 years[2-4].There are no reports of lesions in the fourth ventricle and the whole spine. It needs to be differentiated from other tumors in the spinal canal.

Case report
We reported a case of an 8-month-old child who was found to be unstable and deviated in the previous 2 months. Now the X-ray photograph revealed that the position of the right femur was slightly outside and the previous scoliosis (left), and there was no obvious abnormality. MRI showed that the fourth ventricle of the brain and the whole spine showed short T1 and long T2 signals, and lines and other low signals were seen inside. The lipid suppression sequence showed that the signal of the lesion was significantly reduced. DWI showed that the signal was low. After the enhancement, the lesion did not show obvious enhancement. The brainstem and brainstem showed compression changes (Fig.1, 2). The lipoma may be large in MRI diagnosis, and others are waiting to be discharged. The patient underwent intramedullary extramedullary mass resection of the lumbosacral spinal cord during the first operation. During the operation, it was found that the L2-T11 spinal cord and extramedullary masses and spinal cord tissue had incomplete capsules, fatty appearance, and abundant blood supply. The spinal cord showed obvious changes in compression. After the lesion was removed, the spinal cord was in good integrity. The tumor tissues were taken for pathological examination. The final pathological diagnosis: benign lesions of spinal cord tumors and lipoid tumors on the surface of the spinal cord, considered as fatty fibrous hamartoma . After 1 year, the patient underwent brainstem tumor resection + spinal cord tumor resection + tethered cord lysis + laminectomy. During the operation, the tumor in the fourth ventricle and the remaining tumor in the spinal canal were completely removed. , The pathological tissues taken are sent for examination, and the final pathological examination is the same as the first result. The postoperative recovery was quite good (Fig.3, 4).

关键字 fibrofatty hamartoma; entire spinal canal; child

分类：26. Ultrasound Radiology 影像
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Pediatric thoracic chordoma: a case report and literature review

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An 11-year-old boy presented with an exacerbation of progressive asthma. Chest radiography demonstrated a widened mediastinum. Evaluation by computed tomography and magnetic resonance imaging revealed a thoracic paravertebral mass initially diagnosed as a malignant tumor. Histopathological analysis of the mass revealed a malignant thoracic chordoma. Our imaging results are described, with a comprehensive analysis of imaging findings from the literature.

关键字 Chordoma, mediastinum, thoracic vertebra, pediatric

分类：26. Ultrasound Radiology 影像
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Imaging features and differences among the three primary malignant non-Wilms tumors in children

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Background: The pathology, treatment and prognosis of malignant non-Wilms tumors (NWTs) are different, so it is necessary to differentiate these types of tumors.
Purpose: To review the clinical and imaging features of malignant NWTs and to provide evidence for clinical treatment and follow-up.
Materials and methods: We retrospectively analyzed the CT images of 65 pediatric patients with NWTs from March 2008 to July 2020, mainly including clear cell sarcoma of the kidney (CCSK), malignant rhabdomyoma tumor of the kidney (MRTK) and renal cell carcinoma (RCC). Available pretreatment contrast-enhanced abdominal CT examinations were reviewed by two radiologists. The clinical features of the patients, imaging findings of the primary mass, and locoregional metastasis patterns were evaluated in correlation with pathological and surgical findings.
Results: There were 22 patients with CCSK (14 males and 8 females), 27 patients with MRTK (16 males and 11 females) and 16 patients with RCC (7 males and 9 females). The average diameter of CCSK tumors was 9.8 cm, that of MRTK tumors was 5.9 cm and that of RCC tumors was 5.3 cm. Hemorrhagic necrosis of tumors was present in 14/22 (64%) CCSK patients, 7/27 (26%) MRTK patients and 3/16 (19%) RCC patients. Tumor calcification was present in 3/22 (14%) CCSK patients, 2/27 (7%) MRTK patients and 7/16 (44%) RCC patients. Subcapsular fluid of tumors was present in 9/27 (33%) MRTK patients. Seventy-three percent of CCSK patients demonstrated heterogeneous postcontrast enhancement. Eighty-nine percent of MRTK patients demonstrated various postcontrast enhancements. A total of 88% of RCC patients demonstrated postcontrast enhancement. Metastatic disease of CCSK was present in the lymph node in 2/22 patients (9%), vertebral body in 2/22 patients (9%) and liver and lung in 1/22 patients (5%). Metastatic disease of MRTK was present in the lymph node in 5/27 patients (19%) and the liver and lung in 6/27 patients (22%). Metastatic disease of RCC was present in the lymph node in 3/16 (19%) patients.
Conclusion: NWTs have their own imaging and clinical manifestations. These diagnostic points are different from the clinical and imaging manifestations of WTs, and they are believed to play an important role in clinical work.

关键字 Children. Computed tomography. Renal tumor. Clear cell sarcoma of kidney. Malignant rhabdomyoma tumor of kidney. Renal cell carcinoma. Imaging

分类：26. Ultrasound Radiology 影像
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Combining Deep learning and chest radiographs for diagnosing the etiology of pediatric pneumonia

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Background: Clinical symptoms and inflammatory markers and radiological signs cannot reliably distinguish the etiology of CAP, by combining chest radiographs using a context-fusion convolution neural network (CNN) to study the ability of deep learning for distinguishing the etiology of CAP in children.
Methods: This retrospective study included 1769 cases of pediatric pneumonia (viral pneumonia, n=487; bacterial pneumonia, n=496; and mycoplasma pneumonia, n=786). The chest radiographs of the first examination, C-reactive protein (CRP), and white blood cell (WBC) were collected for analysis. All patients were stochastically divided into training, validation, and test cohorts in a 7:1:2 ratio. Automatic lung segmentation and hand-crafted pneumonia lesion segmentation were performed, from which three image-based models including a full-lung model, a local-lesion model and a context-fusion model were built, two clinical characteristics were used to build a clinical model, a logistic regression model combined the best CNN model and two clinical characteristics.
Results: Our experiments showed that the context-fusion model which integrated the features of the full-lung and local-lesion had better performance than the full-lung model and local-lesion model. The context-fusion model had AUCs of 0.86, 0.88 and 0.93 in identifying viral, bacterial and mycoplasma pneumonia on the test cohort respectively. The addition of clinical characteristics to context-fusion model obtained a slight improvement. Mycoplasma pneumonia was more easily identified compared with the other two types.
Conclusions: Using chest radiographs, we developed a context-fusion CNN model with good performance for noninvasively diagnosing the etiology of community-acquired pneumonia in children, which would help improve early diagnosis and treatment.

关键字 chest radiographs; convolution neural network; community-acquired pneumonia; pediatric; etiology

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Chest radiograph features of community acquired pneumonia in children

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Objective: To analyze the chest radiograph and basic data of children with communityacquired pneumonia, describe the chest radiograph manifestations of hospitalized children with communityacquired pneumonia, summarize and compare the chest radiograph signs and characteristics of children with different pathogenic pneumonia, and evaluate the chest radiograph display of different pathogenic pneumonia, so as to provide the basis for chest radiograph diagnosis of different pathogenic pneumonia and further chest radiograph research data on deep learning support.
Methods: 1769 hospitalized children with CAP in our hospital from 2013 to 2018 were collected, including 487 cases of viral pneumonia, 496 cases of bacterial pneumonia and 786 cases of mycoplasma pneumonia. Record the basic information, collect the first admission chest radiograph, summarize the chest radiograph manifestations of different pathogenic pneumonia.According to the location of the focus of pneumonia, it was divided into left lung, right lung and double lung; according to the imaging characteristics of the focus, it was divided into consolidation, interstitial change and mixed change. According to the location and nature of the focus, the number of cases with cavity, pleural effusion, pleural thickening and hyperventilation in the chest radiograph was counted, and the difference of imaging characteristics in the three kinds of pneumonia was analyzed. Chi square test was used to compare the three pathogens, $P< 0.05$, with statistical significance.
Results: There were 1769 cases of chest radiograph in this study, 719 Cases (40.64%) had consolidation changes, followed by 641 cases (36.24%) with interstitial changes. Consolidation changes with unilateral lungwere found in 551 cases (31.15%),interstitial changes with bilateral lungin 549 cases (31.03%),mixed changes with bilateral lungin 262 cases (14.81%).The chest radiograph analysis of different pathogenic pneumonia showed that the difference of three pathogenic pneumonia in involving bilateral or unilateral lung was statistically significant($P< 0.001$), and the difference between the two groups was also statistically significant($P< 0.001$). Viral pneumonia was more common in involving bilateral lung, and mycoplasma pneumonia was more common in involving unilateral lung; the difference of different pathogenic pneumonia in the left or right lung was not statistically significant. In terms of pathological characteristics, there were significant differences among the three kinds of pathogenic pneumonia in substantive change, interstitial change and mixed change, and there were also significant differences between the two groups ($P< 0.001$). Bacterial pneumonia was mainly consolidation change; viral pneumonia was mainly interstitial change; mycoplasma pneumonia was mainly mixed change. There was significant difference among three kinds of pneumonia in lung hyperventilation ($P< 0.001$). The proportion of hyperventilation in viral pneumonia was significantly higher than that in mycoplasma pneumonia and bacterial pneumonia ($P< 0.001$), and the proportion of cavity in bacterial pneumonia was significantly higher than that in mycoplasma pneumonia and viral pneumonia ($P< 0.001$).
Conclusion: The chest radiograph manifestations of children with communityacquired pneumonia caused by different pathogens have certain characteristics, interstitial

changes of viral pneumonia are more common, lung hyperventilation is more common; consolidation changes of bacterial pneumonia are more common, the right lung is most often involved, the chest radiograph manifestations of mycoplasma pneumonia are diversewithout obvious specificity. However, the chest radiographs of the three pathogens of pneumonia were overlapped, which could be further studied by deep learning

关键字 pneumonia, children, chest radiograph, etiology

分类：26. Ultrasound Radiology 影像
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CT imaging features of pulmonary lymphoproliferative disorders in children

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Objectives: To characterize the pulmonary CT imaging findings associated with Epstein-Barr virus-associated (EBV-associated) pulmonary lymphoproliferative disorders and autoimmune lymphoproliferative syndrome (ALPS), and summarized and analyzed the CT features and clinical manifestations.
Methods: A retrospective review of the data available from 2015 to 2020 of the 20 patients with confirmed diagnosis of ALPS or EBV-associated pulmonary lymphoproliferative disorders underwent chest CT scanning. Evaluated findings included distribution of pulmonary lesions, morphological pattern of appearance, size, presence of thoracic lymphadenopathy, and secondary associated features.
Results: The average age of the subjects was 8.8 years old. Of the 20 patients (six females) studied, 12 had EBV-associated pulmonary lymphoproliferative disorders, 8 had ALPS. All types of major pulmonary lesions were observed in 20 patients. The major pulmonary lesions manifested as nodules, consolidation or ground glass opacity （GGO）. The Major Patterns in CT of patients with EBV-associated pulmonary lymphoproliferative disorders, there were 5 cases (41.7%) identified as single pattern lesions, 5 cases (41.7%) were identified as double pattern lesions, 2 cases (17.6%) were identified as multiform pattern lesions. The Major Patterns in CT of patients with ALPS, there were 4 cases (50%) identified as single pattern lesions, 3 cases (37.5%) were identified as double pattern lesions, 1 cases (12.5%) were identified as multiform pattern lesions. EBV-associated lymphoproliferative diseases have larger nodules and more pulmonary consolidation, while autoimmune lymphoproliferative diseases have slightly smaller nodules and less pulmonary consolidation.
Conclusions: EBV-associated lymphoproliferative diseases and autoimmune lymphoproliferative diseases manifest multiple pulmonary nodules of varying sizes, the size of the nodules may help to distinguish between the two diseases.

关键字 CT, lymphoproliferative diseases, children

分类：26. Ultrasound Radiology 影像
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Imaging Manifestations of Pediatric Coxsackievirus Encephalitis and Review of the Literature

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Objective: To analyse the MRI features of Coxsackievirus encephalitis in children, summarize the imaging characteristics of the disease and provide MRI clue for the clinical diagnosis and prognosis. Methods: Retrospectively analyse the MRI imaging findings of 32 patients who are diagnosed with Coxsackievirus encephalitis, review relative literatures and summarize their MRI imaging features. Results: Totally 32 patients have accepted the MRI and 18 of them have striking manifestations; 10 patients present no abnormality; 3 patients only have bilateral subdural effusion in frontotemporal area; one shows hypomyelination. The 18 lesions symmetrically reveal hypointense on the T1WI, hyperintense on the T2WI and FLAIR, some cases demonstrate restricted diffusion and almost all have bilateral swelling of the cerebral cortex. One has enhancement while other cases don’t. These abnormal signals can relieve after clinical treatments and one case forms encephalomalacia later. 10 of lesions are located in the midbrain, dorsal pons, medulla oblongata and cerebellar dentate nucleus, around the fourth ventricle; also, 11 abnormal areas are in the basal ganglia and thalamus. All abnormalities are almost symmetrical. Conclusion: Coxsackievirus encephalitis has a typical feature presenting the brainstem encephalitis, which the lesions could be located in the rhombencephalon symmetrically, especially in dorsal pons. Whereas lesions in basal ganglia and thalamus, especially in posterior limbs of internal capsule, can also be observed.

关键字 Coxsackievirus encephalitis, viral encephalitis; Pediatrics; Magnetic resonance imaging

分类：26. Ultrasound Radiology 影像
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A Comparative Study of Diffusion Kurtosis Imaging and Diffusion Tensor Imaging in Detecting White Matter Alterations in Children with Obstructive Sleep Apnea Syndrome

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Study Objectives: To compare the ability of diffusion kurtosis imaging (DKI) and diffusion tensor imaging (DTI) in detecting white matter (WM) alterations in children with Obstructive sleep apnea (OSA) in order to find a more sensitive technique to assess WM alterations in OSA children.
Methods: Tract-based spatial statistics (TBSS) analysis was used to compare the DKI derived kurtosis fractional anisotropy (KFA) and DKI derived fractional anisotropy (DKI-FA) as well as DTI derived FA (DTI-FA) maps in 41 drug-naive OSAS children and 32 age and gender matched healthy children.
Results: We found DKI detects WM alterations of OSA children more sensitively than DTI. In addition, the kurtosis parameter (KFA) is sensitive to reveal abnormality in WM regions with complex fiber arrangement, such as corona radiate (CR), superior longitudinal fasciculus (SLF) and inferior fronto-occipital fasciculus (IFOF), while the diffusion parameter (FA) is sensitive to detect abnormality in WM regions with coherent fiber arrangement, such as posterior limb of internal capsule (PLIC), anterior thalamic radiation (ATR) and corpus callosum (CC). Notably, the KFA value in crossing fibers was not only significantly related to the sleep parameters, but also demonstrated the best performance in receiver operating characteristic (ROC) curve analysis.
Conclusions: DKI is useful for evaluation of complex tissue arrangements and providing a sensitive index of pathological changes of brain in OSA. Combining diffusion and kurtosis parameters can provide complementary information, so they should be jointly used to reveal pathological changes and monitor disease progression of OSAS children.

关键字 Diffusional kurtosis imaging, Diffusion tensor imaging, white matter, children, obstructive sleep apnea

分类：26. Ultrasound Radiology 影像
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Hemispheric asymmetry in the anatomical network of the brain in children and adolescents with attention-deficit/hyperactivity disorder

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Objective:
The cognitive and emotional functions of the human brain hemispheres are asymmetrical. The studies have shown that there might be abnormal or absent brain asymmetries in Attention-Deficit Hyperactivity Disorder (ADHD) patients. However, few studies have estimated abnormalities in structural and functional asymmetry in ADHD patients. In our study, the differences in hemispheric asymmetry of white matter network topological properties were explored based on the graph-theoretical analysis between children and adolescents with ADHD and normal controls. The correlation between the asymmetric changes of the structural connection network topological properties and the severity of symptoms was also analyzed.
Methods:
Our study included 29 children and adolescents with ADHD and 27 matched normal controls. Using the diffusion tensor imaging (DTI) technique and the graph-theoretical analysis method, the global and the local parameters Asymmetry Indexes (AIs) of the white matter structure network were calculated. The Mann-Whitney U test was used to evaluate the differences in the clustering coefficient, shortest path length, global efficiency, local efficiency, and small-world network attributes and node efficiency AIs between the ADHD individuals and normal controls. Spearman correlation was used to analyze the correlation between asymmetric changes of topological properties of white matter structural network and SNAP-IV subscores.
Results:
Both the right and left hemispheres of children and adolescents with ADHD and normal controls showed the small-world network attributes ($\sigma > 1$), but there were no significant differences in cluster coefficient, shortest path length, global efficiency, local efficiency, and small-world network attributes AIs between the two groups ($P > 0.05$). There were significant differences between the two groups in the node efficiency AIs of the medial orbital superior frontal gyrus, calcarine fissure and surrounding cortex, and fusiform gyrus ($P < 0.05$).
There was a positive correlation between the node efficiency AI in the medial orbital superior frontal gyrus and the severity of ADHD symptoms on the inattention subscale score ($P < 0.05$). The node efficiency AI in the fusiform gyrus was negatively correlated with the severity of ADHD symptoms on the hyperactivity/impulsivity subscale score ($P < 0.05$). However, there was no significant correlation between the node efficiency AI in the calcarine fissure and surrounding cortex and ADHD symptoms variables($P > 0.05$). The correlations between the node efficiency AIs in these three regions and the opposition subscale score did not reveal significant differences ($P > 0.05$).
Conclusion:
The node efficiency asymmetry of the brain structural connectivity network in children and adolescents with ADHD was abnormal in the medial orbital superior frontal gyrus, calcarine fissure and surrounding cortex, and fusiform gyrus. These differences are associated (at least in part) with the severity of ADHD symptoms. Our

findings provide new insights into the lateralized nature of hemispheric dysconnectivity and highlight the potential for using brain network measures of hemispheric asymmetry as a precursor for ADHD and its clinical features.

关键字 attention-deficit/hyperactivity disorder, children and adolescents, structural asymmetry

分类：26. Ultrasound Radiology 影像
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Lung Ultrasound in Acute Respiratory Distress Syndrome Received Extracorporeal Membrane Oxygenation

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ABSTRACT
Objective: The present study was to assess the lung ultrasound (LUS) score in evaluating the prognosis of pediatric acute respiratory distress syndrome (pARDS) received extracorporeal membrane oxygenation (ECMO).
Methods: A prospective cohort study was performed in pediatric intensive care unit (PICU) of a tertiary university hospital from January 2016 to June 2020. 29 patients with pARDS received ECMO were enrolled. Patients were divided into survival group and non-survival group. LUS score was measured at initiation of ECMO as LUS-0h, then at 24 hours, 48 hours, and 72 hours after ECMO support as LUS-24h, LUS-48h and LUS-72h, as well as weaning ECMO as LUS-wean. The primary outcome was the relationship between LUS scores and mortality within 3 days of ECMO initiation.
Results: The values of LUS-72h and LUS-wean in survival group were significantly lower than that in non-survival group (all $P < 0.05$). Daily fluid balance volume during the first three days of ECMO were significantly correlated with LUS score [24h-0h: r=0.460, P=0.014; 48h-24h: r=0.540, P=0.003; 72h-48h: r=0.589, P=0.001]. The cutoff value of LUS-72h was 24 (AUC 1.000, sensitivity100.0%, specificity100.0%) for predict PICU mortality. Based on the LUS score 24, PICU mortality, the length of PICU stay, vasoactive-inotropic score (VIS), the need of ratio for continuous renal

replacement therapy (CRRT) were significantly different between LUS-72h≥24 and LUS-72h<24 (all P < 0.05).
Conclusions: LUS at 72 hours≥24 is associated with high mortality in pARDS received ECMO.

关键字 lung ultrasound, acute respiratory distress syndrome, extracorporeal membrane oxygenation, child

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Image and pathology features analysis of childhood pilomatricomas

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Purpose To describe the radiological characteristics on CT and MRI of childhood pilomatricomas, and to correlate the radiological findings and pathological features. Materials and methods the radiological finding of 14 pilomatricomas in 13 patients were retrospectively reviewed. Among the 13 patients, six received plain CT, one received plain CT with contrast-enhancement, seven received plain MRI. Results We included 13 consecutive patients with 17 histologically proven pilomatricomas. The tumor were located in head and neck regions(n=13) ,the trunk(n=3),the lower extremities(n=1). Moreover, of lesions in the head and neck, the tumor were in periauricular region(n=5), scalp(n=4), earlobe(n=1),midface region(n=1),neck(n=1). The maximum tumor diameter was in the range of 6-51mm.Most lesions were well-circumscribed, subcutaneous nodules with partial attachment to the overlying skin. Of the 6 patients with 7 lesions evacuated by CT,6 lesions appeared as enhancing soft-tissue masses with varying amounts of calcification in 5 lesions. MR were performed in 7 patients. Homogeneous isointensity on T1-weighted images (T1WI) were show in 4 lesions. On fat-suppressed(FS) T2-weighetd images (T2WI), a ring-like hyperintensity was observed in 4 lesions, reticular hyperintensity in 2 lesions. The ring-like and reticular appearances on MR images respectively corresponded to tissue capsule edematous stroma on pathology. Conclusions Pilomatricomas perform tissue-soft density with different patterns of calcifications on CT images. MRI typical features of pilomatricomas include reticular and ring-like hyperintensities on fat-suppressed T2WI. Radiological findings are well correlated with pathological findings.

关键字 Pilomatricoma; Calcifying epithelioma of Malherbe; Tomography, X-ray computed; Magnetic resonance imaging

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Comprehensive assessment of motor function after hemispherectomy in children with refractory epilepsy

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OBJECTIVE: Hemispherectomy (HS) is a group of effective surgical procedures for the treatment of refractory epilepsy due to diffuse hemispheric lesions. Postoperatively, seizures are well controlled and different types and degrees of altered motor function can be seen. This result highlights the strong plasticity of the brain, which can undergo functional reorganization and structural remodeling after extensive damage, especially in young children. Multimodal MRI is currently considered to be the best method for the comprehensive assessment of motor function after hemispherectomy, as it allows for the combined analysis of structural and functional brain and related neuroimaging features to reveal the mechanisms of motor function alterations. The purpose of this paper is to summarize the progress of research on the application of multimodal MRI techniques in the prognosis of motor function after cerebral hemispherectomy and to provide new insights into the complex mechanisms of motor function alterations, which can help the development of postoperative rehabilitation strategies.
Methods: In large domestic and international databases such as Pubmed, Springer Link, China Knowledge Network and Wanfang, the keywords "Hemispherectomy; Magnetic resonance imaging; prognosis" or Chinese were searched for in MeSH. The keywords "hemispherectomy; magnetic resonance imaging; prognosis" were used to review the relevant literature on the application of MRI in motor function after hemispherectomy from January 2007 to February 2021, and the relevant literature was sorted by Medical Literature King and excluded, mainly referring to the domestic and foreign literature within the last 5 years.
RESULTS: Forty-seven studies were finally included in the literature, including 38 in English and 9 in Chinese, with a foreign language citation rate of 81% and 43% of the literature cited in the last 3 years. Currently, multimodal magnetic resonance imaging provides a good measure of neuroimaging indicators in children after hemispherectomy, and several scholars have also used diffusion tensor imaging and voxel-based morphometry in recent years to analyze postoperative cone bundle and extravertebral bundle diffusion indicators and fiber volume changes in children. Diffusion tensor imaging reveals a strong correlation between changes in motor function and neurological remodeling of the brain in children after hemispheric surgery through microstructural changes in white matter fiber tracts. Another study using resting-state and task-state functional magnetic resonance revealed that the seven classical brain networks in the contralateral hemisphere were preserved after hemispheric surgery, and the enhanced connectivity between the networks was strongly correlated with improved motor function.
CONCLUSIONS: Diffusion tensor imaging is currently the most widely used and established technique for postoperative motor function in the hemispheres, while task-state functional MRI is faster and more direct but has limitations in the analysis of younger children (≤3 years), and voxel-based morphological measurements can exclude age and disease course factors but are difficult to assess the development of postoperative changes in the neural nuclei of the brain. Resting-state functional magnetic resonance imaging allows observation of postoperative brain network changes and more accurate evaluation of the degree of functional remodeling.

Diffusion tensor imaging is the only method that can detect neural microstructural changes noninvasively, and its convenience and stability are helpful in explaining the neural remodeling mechanisms related to motor function in children after hemispheric surgery. Therefore, the combination of multiple MRI sequences can be useful for a comprehensive analysis of the prognosis of motor function in children after hemispherectomy, as well as for the assessment of outcome and functional trends.

关键字 大脑半球切除术；运动功能；多模态磁共振；儿童

分类：26. Ultrasound Radiology 影像
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Aberrant interhemispheric structural and homotopic functional connectivity in children with spastic cerebral palsy

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Background Prior studies have shown corticospinal tract (CST) abnormalities in spastic cerebral palsy. However, few studies to date have examined interhemispheric neural connectivity in spastic cerebral palsy in vivo. The purpose of this study was to investigate alterations of interhemispheric structural and functional connectivity in children with spastic cerebral palsy. **Methods** Thirty-seven participants with spastic cerebral palsy and eighteen age- and gender- matched controls were enrolled in this study and underwent MRI (including conventional T1-weighted imaging , resting-state functional MRI and participants aged ＞3 years have underwent 30-direction DKI sequence) , fine motor function measure scale(FMFM) and gross motor function classification system (GMFCS) testing. DKI data were analyzed with automated fiber quantification (AFQ) to identify the callosum forceps major tracts and callosum forceps minor tracts, mean kurtosis (MK) and fractional anisotropy (FA) were measured in the callosal tracts. Interhemispheric functional connectivity was derived with analyses of voxel mirrored homotopic connectivity (VMHC). **Results** At a group level, significant differences between patients and controls were seen in callosum forceps major and callosum forceps minor. MK decreases and FA increases were detected when comparing spastic cerebral palsy patients to controls. Higher MK values at nodes 11-13 along the callosum forceps major correlated with lower GMFCS scores, while lower FA values at nodes 8-12 along the callosum forceps major correlated with lower GMFCS scores and higher FA values at nodes 7-12 along the callosum forceps minor correlated with lower FMFM scores. The resting-state functional MRI has revealed reductions of VMHC associated with spastic cerebral palsy in brain regions of the precentral gyrus, postcentral gyrus, paracentral lobule, medulla, middle occipital gyrus, calcarine gyrus, cuneus, thalamus, precuneus and inferior parietal lobule. Additionally, interhemispheric functional connectivity of the cuneus, calcarine, middle occipital gyrus and medulla were positively correlated with GMFCS scores, while interhemispheric functional connectivity of the middle occipital gyrus, cuneus and calcarine were positively correlated with FMFM scores. **Conclusions** These findings provided direct evidence confirming and extending the view of impaired interhemispheric neural communications mediated by corpus callosum, providing a new perspective for examinations and understanding the pathophysiology of spastic cerebral palsy.

关键字 diffusion kurtosis imaging; voxel mirrored homotopic connectivity; cerebral palsy; corpus callosum; white matter; motor impairment

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Comprehensive myocardial contractility in children with Kawasaki disease by cardiac magnetic resonance in a large single center from Shanghai, China

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Objective: Children with Kawasaki disease (KD) and coronary artery lesions (CALs) can develop myocardial ischemia, fibrosis and abnormal contractility. We aimed to assess the association between myocardial mechanic deformation with myocardial fibrosis, ischemia and CALs.
Methods and Results: Totally 76 KD and 20 healthy volunteers received cardiac magnetic resonance (CMR). Peak systolic left ventricular longitudinal, radial, and circumferential strain and strain rate (LVSL, LVSR, LVSC, LVSRL, LVSRR, and LVSRC), along with late gadolinium enhancement (LGE), perfusion deficit and CALs in related segment were analyzed. The KD group was subdivided by CALs, perfusion and LGE results. Strain results were compared with controls and in subgroups.
Results: Cardiac fibrosis and ischemia were not confined in territory of CALs. In global analysis, strain and strain rate were lower in KD group, especially in subgroup with LGE and perfusion deficit. In segmental analysis, LVSR, LVSC, LVSL and LVSRR decreased in giant aneurysm group. Lower LVSR (20.369 ± 10.603% vs 26.071 ± 12.349%) and LVSC (-13.37 ± 5.365% vs -15.847 ± 5.778%) were observed in thrombosed segments. The strain and strain rate were all lower in segments with LGE and perfusion deficit. No obvious difference was found between groups with and without stenosis. LVSR had a better ability to identify giant aneurysm, thrombosis, stenosis, perfusion deficit and LGE.
Conclusion: We detected lower strain values in KD patients, more pronounced in segments with aneurysm, thrombi, LGE and perfusion deficit. LVSR is useful to discern patients with higher risk.

关键字 Cardiac magnetic resonance, feature tracking, Kawasaki disease, myocardial fibrosis, coronary artery aneurysm, thrombosis

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Calcium Salt Deposit Sign—Chronic Kidney Disease-one case report

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A 3-year-old male child presented vomiting and abdominal pain with no obvious inducement half a month ago, with shortness of breath. His parents said the child had been diagnosed with chronic kidney disease (stage 5) for more than two years, with secondary hyperparathyroidism, and was treated regularly by peritoneal dialysis. The physical examination revealed that the breath sounds of both lungs were reduced, and the abdomen had no tenderness. A plain CT scan of the lungs and abdomen was performed, we found diffuse ground glass shadows in both lungs were found and multiple calcifications in the heart, esophagus and stomach wall. Further whole-body bone scan also found calcium salt deposits in both lungs and stomach. Skeletal changes caused by chronic kidney disease are more common in the limbs, but the lungs and stomach are extremely rare. The lungs and stomach of this child show typical signs of calcium salt deposition.

关键字 Chronic Kidney Disease

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Inverted Glass Sign-Ectopic Liver Disease-one case report

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A 12 - year - old boy presented abdominal pain and weak urination with no obvious inducement one month ago. Routine urinalysis showed no abnormalities. Physical examination reveals a dense mass in the lower abdomen. Abdominal MRI and CT enhancement scan found that the upper abdomen liver volume was significantly smaller, and the lower abdomen found a solid mass, with cord of soft tissue and vascular connected between each other. Further DSA examination confirmed extrahepatic portal shunt, with absence of intrahepatic portal vein, and ectopic liver. The child should be follow-up and did not require surgical treatment at once. Portal shunt disease is common, but it is extremely rare to have ectopic liver and intrahepatic portal vein absence, which is worth learning.

关键字 Ectopic Liver Disease

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The clinical and radiological features of pediatric adrenal cortical carcinoma

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Purpose Pediatric adrenal cortical carcinoma (ACC) is rare. The aim of this research is to analyze the clinical and radiological features of ten cases with ACC, and compare these features with the benign/uncertain malignant potential ones.
Materials and Methods Twenty cases (twenty-one masses) of adrenal cortical tumor in our institution, from October 2011 to October 2016, were collected and analyzed. Ten cases (eleven masses) were pathologically proven ACC, four uncertain malignant potential cortical tumor, and six adenoma (two suspected) were included. Sixteen cases were performed CT scans, ten MR scans (seven with DWI), and seven cases underwent both CT and MR scans. These masses were divided into the malignant and benign/uncertain malignant potential group. The clinical and radiological findings of carcinoma and its counterpart were compared. The independent samples T test and Fisher exact test (SPSS Version 17.0) were used for statistical analysis.
Results Eleven complained of precocious puberty, ten with elevated level of hormones (mainly androgen); the sex ratio is 3:2. In the malignant group, the age ranged from 18 month to 12 years old, with the median age was 3 years old; 90% of patients were less than five years old. Sixty percent suffered from precocious puberty, 30% manifested abdominal mass; 80% manifested the elevation of hormone level. While in counterpart group, the median age was 5 years old (7 month to 13 years old), the rate of precocious puberty was 50%, and only two with the elevated hormone level. The maximal diameter of malignant (7.35±3.08cm) was larger than counterpart group (3.87±2.11cm). All the masses showed gradually enhanced pattern. The unenhanced CT values, calcification rate, and haemorrhage/necrosis rate of malignant group are significant higher than the benign/uncertain malignant potential group ($p<0.05$). Conversely, CT value of artery, and portal vein phase had no significant differences between these two groups. On T1WI, the parenchyma showed homogeneous mainly iso-signal intensity. On T2WI, the masses showed heterogeneous hyper- signal intensity, with necrosis. Six cases (four carcinoma) of them showed reticular enhancement. The ADC values of ACC (1.01±0.09 mm2/s) were significant lower than that of its counterparts (1.23±0.04 mm2/s) ($p<0.05$). Metastasis were detected in six cases (54.5%) of carcinoma, two with recurrence; lung (6 cases) was the most metastatic site, followed by liver (2 cases), lymph node (1 retroperitoneum, I hilum of right lung).
Conclusion The clinical and radiological features of pediatric adrenal cortical carcinoma are different, compared with its counterparts. ACC occurs younger; is more likely with elevated hormone level, larger and more commonly accompanied by calcification, haemorrhage/necrosis; enhances more heterogeneous and with lower ADC values; recurs easily and has high metastasis rate (54.5%), lung is the most common metastasis site.

关键字 Adenoma, Uncertain malignant potential adrenal cortical tumor, Adrenal cortical carcinoma, Apparent diffusion coefficient

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Different Levels of Radioactivity Uptake in the Tumour Nidus are Not Accidental: Quantitative Bone Scintigraphy in Osteoid Osteoma

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OBJECTIVE—To investigate factors related to different levels of radioactivity uptake in the tumour nidi of osteoid osteoma during bone scan.
MATERIALS AND METHODS—Imaging data of 22 children (16 males and 6 females; age, 7.64±3.97 years [range, 2–13 years; median, 8 years]) with pathologically confirmed osteoid osteoma were retrospectively analysed (plain X-ray, CT, and bone scan). The total radioactivity count ratio (A ratio) and the maximum radioactivity count ratio (B ratio) in the region of interest on the affected side and in the corresponding region on the healthy side were measured though a 99mTc-MDP bone scan, while the nidus area (mm2), nidus calcification area (mm2), nidus calcification ratio and CT attenuation of nidus calcification (HU) were measured by the CT imaging; the correlation between these measurements was analysed.
RESULTS—The A ratio (2.76±1.11; range, 1.07–5.43; median, 2.58) and the B ratio (2.70±1.27; range, 1.08–5.65; median, 2.56) were significantly correlated (P=0.000). The B ratio increased or decreased only with an increase or decrease in the nidus calcification ratio (0.49±0.10; range, 0.37–0.67; median, 0.46) (P=0.001). However, there was no significant correlation of the B ratio with age, nidus area, nidus calcification area, and CT attenuation of nidus calcification.
CONCLUSION—Quantitative bone scan analysis can reflect the activity of the tumour nidi and hyperplastic bone in cases of osteoid osteoma. Radioactivity uptake in the tumour nidi increases and decreases with the calcification rate.

关键字 Osteoid Osteoma; Bone Scintigraphy; CT; Calcification

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Role of Multidetector Spiral CT in the Preoperative Evaluation of Bronchopulmonary Sequestration in Children

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Background To discuss the value of various CT signs in the diagnosis and preoperative assessment of bronchopulmonary sequestration (BPS) in children.
Method forty-two patients in the age range of 5 days to 11 years suspected of having BPS were included in this study. All patients underwent multidetector spiral CT and were confirmed by surgery and pathology. Twenty-two were intralobar sequestrations (ILS) and twenty were extralobar sequestrations (ELS). The site and shape of the lesion, angioarchitecture, lung parenchyma, airway and pleural abnormalities, co-existent congenital anomalies were analyzed and correlated with the surgical and pathological findings.
Results Of the 22 patients with ILS, 18 were located in the left lower lobe and 4 were located in the right lower lobe. Of the 20 patients with ELS, 14 were located in the left posterior costodiaphragmatic sulcus, 1 was located in the right posterior costodiaphragmatic sulcus, 2 was located within the left postero-inferior mediastinum, 1 was located in the left postero-inferior mediastinum and extended downward through the diaphragm, 2 was located within the right postero-inferior mediastinum. Thirty-six cases appeared as homogenous or inhomogenous masses, 6 cases manifested as tubular or branching structures. Emphysematous changes were revealed in 21 cases. Lung parenchyma infiltration or consolidations were found in 14 cases. Pleural changes were detected in 18 cases. CT detected aberrant systemic arteries in all patients and identified venous drainage in 34 cases. Eighteen patients were associated with other congenital anomalies. The differences in shape of the lesion, air within the mass, pleural changes, venous drainage, and coexistent congenital pulmonary airway malformation between intra- and extralobar sequestration were statistically significant, P value was 0.000, 0.000, 0.012, 0.001 and 0.047 respectively. Other CT signs between intra- and extralobar sequestration showed no statistical difference.
Conclusion Spiral CT reveals the site and shape of the lesion, angioarchitecture, lung parenchyma, airway and pleural changes, and co-existent congenital anomalies that allow a diagnosis of BPS. This information is helpful in differentiating intralobar sequestration from extralobar sequestration and in planning the procedure of surgical operation.

关键字 CT，children, bronchopulmonary sequestration

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AI generates better and less varied Bone age evaluation values than individual doctor

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Bone age (BA) estimate has large inter-observer variablilities ranging from 0.6-1 years. To valid the BA estimate variablity between AI and individual doctor, a deep learning BA model with 11226 images was implemented and generate AI BA on a testset with 1246 cases from our hospital. Disputed cases outside 96% LOA of manual and automated difference were extracted and rerated by aother doctor. The average of original report and rerated BA was regarded as a new manual BA value. Meanwhile, 7798 continuous BA radiologic reports data from RIS system of our hospital were exported to analyze inconsistent BA values report (between junior and auditing doctor). Compared with BA value from a single doctor, new manual BA (10.73 years) combined orignial report BA and rerated BA was closer to mean of AI BA (10.70 years) than report BA (10.59 years) of 69 disputed cases ($P<0.01$). The proportion of disputed cases where the new BA agreed better with AI BA than original single report BA was 65.2% (45/69). In 2134 inconsistent report (27%), the difference of initial and auditing report BA reached 0.7 years. AI would have a better Bone age estimation than individual doctor.

关键字 AI, bone age, interobserver variability

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Evaluation of Duchenne muscular dystrophy :comparison of shear wave elastography, Dixon MRI and clinical motor function

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[objective]
To explore the correlation between average shear wave velocity (ASWV), muscle fat fraction (MFF) and clinical motor function by analyzing the results of shear wave elastography (SWE) and Dixon imaging of right gluteus maximus muscle in patients with Duchenne muscular dystrophy (DMD).
[Methods]
12 patients with DMD diagnosed by genetic test in Shenzhen Children's Hospital and 12 age-matched healthy children from January 2020 to June 2021 were selected.The right gluteus maximus muscles of the subjects were imaged by SWE and Dixon respectively. Mann-Whitney u test was used to compare the difference of ASWV between the case group and the control group. Spearman rank correlation analysis was used to analyze the correlation between ASWV, MFF and motor function in the case group.
[Results]
The ASWV of the right gluteus maximus muscle in the case group and the control group was 2.20m/s and 2.71m/s respectively,there was significant difference in ASWV between the case group and the control group（Z=-1.99，P＜0.05）.In case group, MFF was (57±18)%,there was no correlation between ASWV and MMF in the case group（p=0.24，r=0.37）.The results of 30-step walk, Gower score, 4-stair climb and 6 minute walk were 15.50（12.00-17.23）s,10.00（2.45-20.00）s,4.50（2.00-8.00）s and 373.75（211.25-503.75）m respectively.ASWV was positively correlated with 30-step walk (r=0.62，P=0.03). MFF was positively correlated with Gower score (r = 0.72, P= 0.01), 30-step walk (r=0.60, P=0.04), 4-stair climb (r=0.67, P=0.02),while negatively correlated with 6-minute walking test (6MWT) (r=0.68, P=0.02).
[Conclusion]
It's feasible and accurate to measure the muscle stiffness with SWE. Both ASWV and MFF have a certain correlation with clinical motor function which are the ideal biomarkers to evaluate disease progression and reflect the effect of treatment.

关键字 Muscular Dystrophy, Duchenne; shear wave elastography; Dixon MRI; motor function assessment

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Evaluation of Fetal Spinal Anatomy and Vertebral Malformation with 3T Magnetic Resonance Three-dimensional T2-STAR FFE Sequence

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Objective To analyze the value of 3T magnetic resonance 3D-T2 star FFE sequence showing fetal spinal anatomy and vertebral malformations. **Methods** This study included 21 middle and late pregnant women whose prenatal ultrasound showed abnormal fetal vertebral bodies or unclear spine parts. The gestational age was 25.0-37.4 weeks, with an average of (30.1±3.6) weeks. All fetuses underwent corresponding spinal MRI examination, and the scanning sequences included three-dimensional T2 star fast field echo sequence (3D-T2 star FFE), two-dimensional single shot spin echo sequence (2D SSH TSE) and two-dimensional balanced fast field echo sequence (2D BTFE). The image quality of each segment of the spine of the three sequences was scored by two diagnosticians, and the difference in scores between the sequences was compared using the non-parametric Friedman test. An intermediate technician delineated the region of interest (Region of Interest ROI) for all cases and calculated the signal difference ratio *SI of the corresponding vertebral bodies and intervertebral discs in the cervical, thoracic and lumbar segments of the three sequences respectively to evaluate image contrast. The one-way analysis of variance was used to compare whether the difference in signal difference ratio of each sequence was statistically significant.**Results** The differences of image quality scores of each spinal segment in the three sequences images were statistically significant ($P < 0.05$). The pairwise comparison indicated that the image quality of the cervical spine showed by 3D-T2 star FFE was better, and the difference was statistically significant as compared with the scores of 2D SSH TSE and 2D BTFE sequences.，and quality score of thoracic and lumbosacral vertebra images of BTFE sequence was higher than that of SSH TSE sequence. For the display of fetal cervical spine, the * SI values of 2D BTFE and 3D-T2 star FFE sequences were higher than that of 2D SSH TSE sequence, and the difference was statistically significant. There was no statistical difference in * SI of fetal thoracic and lumbar spine sequences. **Conclusions** 2D BTFE and 3D-T2 star FFE sequences under 3 T magnetic resonance performed well on fetal vertebral bodies imaging. However, 3D-T2 star FFE was able to show more anatomical details of the spine, without being affected by fetal position, And the scanning time is short, which can reduce the influence of fetal movement on image quality ,thus having high prenatal diagnosis value for vertebral body alformations. It can be used as an important supplementary sequence for fetal spine scanning imaging during clinical magnetic resonance scanning.

关键字 fetal spine; magnetic resonance imaging; T2 star fast field echo sequence

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Clinical and Imaging Analysis of 15 Death Cases of Influenza-Associated Encephalopathy in Children

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Objective To summarize the clinical and imaging characteristics of influenza-associated encephalopathy (IAE) in children, and establish a correlation model between IAE imaging scores and survival time in order to improve the accuracy and timeliness of IAE diagnosis. **Methods** The clinical data, laboratory examinations, and head CT of death cases of influenza-related encephalopathy in Shenzhen Children's Hospital from March 2016 to September 2020 were retrospectively analyzed, and a large number of previously reported cases were compared. The children were divided into groups according to the increase, normal and decrease of six laboratory indexes such as leukocyte and blood glucose. The Mann-Whitney U test was used to compare the difference of survival time between the increase group and the normal group, and the Kruskal-Wallis H test was used to compare the difference of survival time between the increase group, the normal group and the decrease group. The imaging scoring method was established by the number of affected parts and the cumulative score of complications. The correlation between imaging score and survival time of children with IAE was evaluated by Spearman correlation analysis. **Results** There were 15 deaths from influenza-related encephalopathy, with an average age of 4.57 (±2.44) years old. There were 14 cases of influenza A (H1N1) and 1 case of influenza B. The clinical symptoms are high fever (86.6%), vomiting (53.3%), convulsions (66.6%), and disturbance of consciousness (93.3%). There was no significant difference in survival time between the groups with elevated, normal and decreased six laboratory indexes such as leukocyte and blood glucose ($P > 0.01$). CT scan of 13 children showed diffuse swelling of bilateral cerebral hemispheres in 11 cases, involving brain stem in 7 cases, cerebellum in 4 cases and thalamus / basal ganglia in 5 cases. Cerebellar tonsillar hernia occurred in 2 cases and subarachnoid hemorrhage in 4 cases. The imaging scores were in accordance with the normal distribution and scores of each case were 0-6 points, with a median of 3 points. The imaging score was correlated with the time of death ($r=0.698$, $P<0.01$). The main difference between this study case and other reported cases is the incidence of prodromal symptoms. The incidence of fever and vomiting in children in Shenzhen is higher, while the incidence of upper respiratory tract infection symptoms is lower. **Conclusion** The prodromal symptoms and neurological symptoms of this group of children with influenza-related encephalopathy are fever, vomiting and convulsions, and disturbance of consciousness. For children with high fever, vomiting, and disturbance of consciousness, if head CT shows diffuse cerebral edema involving multiple parts, especially symmetrical swelling of the thalamus and brainstem, we should be alert to the possibility of IAE. There is a good correlation between imaging scores and survival time of children. The higher the imaging score, the shorter the survival time of children, which helps clinicians to judge the severity of the disease.

关键字 Child; Encephalopathy; Influenza; Imaging; Death

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Identification model of pathogen of necrotizing pneumonia based on machine learning

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Objective: Streptococcus pneumoniae and Mycoplasma pneumoniae pneumonia are two common pathogens of lung necrosis. The purpose of this study was to explore the ability of Radiomics to distinguish the two pathogens causing lung necrosis based on plain scan CT imaging features.
Materials and methods: 86 cases of lung necrosis with early pulmonary consolidation were included according to the standard of sodium discharge. Imaging images and clinical features were collected. RadCloud was used to segment the lesions in CT scan manually, and 1409 radiomics features were extracted. In order to reduce redundancy, we use minimum absolute contraction and selection operator (LASSO) method for eigendimension reduction. The model based on Radiomics features and the composite model based on imaging and clinical features were established respectively, and the two models were compared. Random forest (RF), support vector machine (SVM) and logistic regression (LR) are three machine learning algorithms used to build machine learning models. To evaluate the recognition effect, area under the receiver operating characteristic curve (AUC), sensitivity, specificity and other indicators were used in the validation cohort.

Results: The minimum absolute contraction and selection operator (Lasso) method was used for feature dimension reduction, and eight Radiomics features with the best correlation coefficients with lung necrosis were identified. Three kinds of models were established: the model based on Radiomics, the model based on clinical features, and the composite model based on imaging features and clinical features. Random forest (RF), support vector machine (SVM) and logistic regression (LR) are three machine learning algorithms used to build the models. The values of AUC, F1-scores and RF in the composite model are 0.795 and 0.78 respectively in the training queue, and 0.774 and 0.81 respectively in the test queue.
Conclusion: The machine learning model RF based on the combined model of imaging and clinical features extracted from the area of interest at the early stage of pulmonary necrosis is helpful for the identification of two pathogens (Streptococcus pneumoniae pneumonia and Mycoplasma pneumoniae pneumonia).

关键字 Streptococcus pneumoniae, Mycoplasma pneumoniae, Children, Radiomics, Machine learning

分类：26. Ultrasound Radiology 影像
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Imaging Features of Graft Versus-Host Disease with Multiple System Impairment after Allogeneic Hematopoietic Stem Cell Transplantation in Children

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Background Allo-genetic hematopoietic stem cell transplantation (allo-HSCT) is an increasingly available treatment option for patients with various hematologic, oncologic and immunologic diseases. As one of the deadly complications associated with this treatment, the diagnosis of graft-versus-host disease (GVHD) is still difficult for it can mimic other HSCT complications such as infection, infarction and drugs-associated toxication. This study aimed to summarize the imaging features(include X ray, CT and MRI) of graft versus-host disease with multiple system impairment after allogeneic hematopoietic stem cell transplantation in children, and to improve the understanding of the disease. **Methods** The clinical and imaging data from 12 patients with GVHD after allogeneic hematopoietic stem cell transplantation during November 2016 to September 2020 were analyzed retrospectively. **Results** Respiratory and circulatory system involvement was found in 9 cases, including 7 chronic GVHD. Chest CT scan showed strip shadow in 5 cases, patchy consolidation in 3 cases, ground-glass opacity in 2 cases, nodular shadow in 1 case, incomplete aeration in 2 cases(mosaic perfusion), bronchial wall thickening in 2 cases, bronchiectasis in 1 case(signet ring sign), interstitial pulmonary edema in 1 case, pleural effusion in 2 cases, pericardial effusion in 1 case, bronchiolitis obliterans in 1 case and pulmonary fibrosis in 1 case. Central nervous system involvement was found in 1 case. The cerebral cortex, subcortical white matter and deep nuclei were involved. Lesions showed hypointensity on T1WI and hyperintensity on T2WI, FLAIR, DWI and ADC. Digestive system involvement was found in 3 cases. Repeatedly intestinal obstruction, partial intestinal wall thickening and bowel loops fluid filled were found in 2 cases. Swollen lymph nodes were found in 1 case, diffuse dilated bowel loops, blurred surrounding fat space and few ascites was found in 1 case. There was 1 case with transplantation-associated thrombotic microangiopathy and 1 case with intracranial hemorrhage and cerebral hernia. 4 of 12 cases eventually died due to multiple organ failure. **Conclusions** The imaging features of GVHD after allogeneic hematopoietic stem cell transplantation in children are various and latent. The risk of fatal complications increases when vital sites involved. Radiographic examination can provide reliable evidence for disease evaluation and biopsy location. Children showed slightly imaging features with history of transplantation should be paid much attention to the condition changes.

关键字 Allogeneic hematopoietic stem cell transplantation; Graft versus-host disease; Multiple system; Imaging diagnosis; Children; Tomography; X-ray computed; Magnetic resonance imaging

分类：26. Ultrasound Radiology 影像
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Clinical application of digital guide plate in precise osteotomy and fixation of cubital varus deformity in children

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Objective：To explore the clinical application effect of digital guide plate in precise osteotomy and reduction and internal fixation during cubitus varus correction in children based on 3D printing technology.
Method of this study is to collect 16 patients with infantile complex elbow varus, randomly divided into control group and experimental group and control group (n = 8) in children with elbow orthotics and traditional experimental group (n = 8) in the 3 d printing digital guide auxiliary in pediatric elbow diorthosis under, its digital guide is designed by 3 d reconstruction bilateral upper limb bone model, Multidirectional osteotomy plane was set to complete the design of osteotomy guide plate. The software simulated osteotomy and reduction, and obtained the reduced bone block. The reduction guide plate was made according to its surface, and the kirschner wire implantation path was planned to design the reduction and internal fixation guide plate. Postoperative X films were reviewed to observe the implantation of Kirschner wire, and the lifting Angle of the affected side was measured. The difference of the lifting Angle, whether the implantation of Kirschner wire was offset, the range of flexion and extension, and whether there were complications were compared between the two groups to evaluate the efficacy.
Results：1. The difference between the lifting Angle of the elbow and the healthy side after operation ranged from 0.5 ° to 4.0 °, with an average of 1.9°; In the experimental group, it was (0.2 ~ 1.0) °, with an average of 0.5°; 2. Postoperative observation of 1 case of Kirschner wire implantation deviation in the control group, and no kirschner wire implantation deviation in the experimental group; 3.16 cases were followed up for 3-16 months, and there were no complications such as distal internal rotation deformity of humerus and ulnar nerve palsy. At the last follow-up, the efficacy of the two groups was assessed by elbow Flynn scoring standard, and the control standard was: excellent in 4 cases, good in 3 cases and fair in 1 case; Standard evaluation of the experimental group: excellent 6 cases, good 2 cases;
Conclusion：The application of digital guide plate can achieve surgical precision osteotomy, reduction and internal fixation, and provide a new surgical scheme for preoperative personalized evaluation and accurate planning of cubitus varus correction in children, and provide guidance for intraoperative comprehensive navigation treatment.

关键字 cubital varus in children; Digital guide plate; 3D printing

分类：26. Ultrasound Radiology 影像
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3D 3D digital guide assisted pedicle screw fixation for congenital scoliosis in children

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Objective: This study was conducted to explore the therapeutic effect of 3D digital guide plate assisted pedicle screw fixation in children with congenital scoliosis by combining medical digital modeling and 3D medical imaging technology.
Methods: A retrospective analysis was performed on the data of 25 pediatric patients with congenital scoliosis who were hospitalized from December 2018 to December 2020. Among them, 14 patients underwent traditional freehand screw fixation from December 2018 to mid-December 2019 (traditional group). From December 2019 to mid-December 2020, 11 patients were treated with personalized 3D digital guide plate assisted screw internal fixation (digital guide plate group). The two groups were compared in the perioperative period, postoperative recovery effect (follow-up) and imaging data. Results: 1. Patients in both groups completed surgery, and no nerve injury was observed during intraoperative nerve monitoring. The operative time and intraoperative blood loss of the digital guide group were significantly better than those of the traditional group, with statistically significant differences ($P<0.05$). 2. The Cobb Angle of the digital guide group was significantly lower than that of the traditional group, and the correction rate was better than that of the traditional group, with statistical significance ($P<0.05$). Image data showed that there was no screw failure or loosening in the digital guide group, while there were 2 screw placement failures in the traditional group.
Conclusion: 3D digital guide plate can effectively assist the treatment of congenital scoliosis in children, realize the precise implantation of pedicle screws, and provide new ideas and methods of digital medicine for the treatment of congenital scoliosis in children.

关键字 3D printing; digital guide plate; congenital scoliosis in children; internal fixation

Cardiology

心脏心血管

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Alteplase for treating thrombosis in Kawasaki disease Patients with CAA

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Objective: The most severe complication associated with giant coronary aneurysm in children with Kawasaki disease is ischemic cardiomyopathy (ICM) caused by thrombolysis. Effective thrombolytic therapy has a significant impact on patients' quality of life in long term. Methods: To compare effects of three anti-thrombotic treatment for KD children with central thrombus in coronary aneurysm. These patients were treated in pediatric cardiology department of Shengjing hospital, China medical university, between 2010 Jun to 2021 May,. Results: There were 7 male patients (9 times) who had CAA complicated with central thrombosis. Methods 1 : 2 patients with ICM caused by LAD thrombosis were treated with combination of 2 anti-platelet agents warfarin orally. In the following ups, patient #1 died 2 years later and patient #2 continued to have ICM. Methods 2: 3 patients were treated with combination of 2 anti-platelet agents plus intravenous administration of heparin Q8H for one week, followed by oral warfarin. Methods 3: Total 4 patients were treated. All succeed. Conclusion: 1. In KD patients with CAA complicated with low density thrombosis convex to the lumen less than a month, it is safe and effective to treat patients using intravenous alteplase once, followed by intravenous heparin treatment for one week and oral warfarin. Alteplase does not have to be rigidly within 12 hours of clot formation. 2. Combination of anticoagulant and anti-platelet aggregation is effective in the treating low density thrombosis. 3. Warfarin combined with anti-platelet aggregation therapy has little effect on thrombosis.

关键字 children; Kawasaki disease; coronary aneurysm; thrombus; alteplase; heparin; warfarin; prognosis

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Treatment of thrombosis in coronary aneurysm in KD children with alteplase

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Objective: The most severe complication associated with giant coronary aneurysm in children with Kawasaki disease is ischemic cardiomyopathy (ICM) caused by thrombolysis. Effective thrombolytic therapy has a significant impact on patients' quality of life in long term. Methods: To describe the effects of alteplase treatment for KD children with central thrombus in coronary aneurysm. These patients were treated in pediatric cardiology department of Shengjing hospital, China medical university, between 2020 Jan to 2021 May. Results: There were 4 male patients (6 times) who had CAA complicated with central thrombosis. Methods 1 : 3 patients were treated with combination of 2 anti-platelet agents plus intravenous administration of heparin Q8H for one week, followed by oral warfarin. Methods 2: Total 4 patients were treated. All succeed. Conclusion: 1. method 1 was only better in KD patients with CAA complicated with low density thrombosis, while those high echo thrombosis and convex to the lumen less than a month, it is safe and effective to treat patients using intravenous alteplase once, followed by intravenous heparin treatment for one week and oral warfarin. Alteplase does not have to be rigidly within 12 hours of clot formation.

关键字 children; Kawasaki disease; coronary aneurysm; thrombus; alteplase; heparin; warfarin; prognosis

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Clinical characteristics and prognostic factors of Takayasu arteritis in children

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Objective: This study aims to analyze the basic data, clinical manifestations, laboratory examination and imaging data of Takayasu arteritis (TA), summarize its clinical characteristics and prognosis, in order to early diagnosis and treatment, reduce related complications and improve the prognosis of children.
Methods: Total 31 TA children were collected and retrospective analyzed from pediatric department of Shengjing hospital, china medical university between 2016 Jan and 2020 Dec.
Results: 1. Basic data: there were 31 children with TA, including 21 girls (67.7%) and 10 boys (32.3%). X2=3.90, P=0.048Showed significantly difference. The average age of diagnosis was 9 years (3 months-12 years). 2. The clinical manifestations of TA Group: 15 cases (48.4%) had hypertension symptoms, and this part of the children showed renal artery involvement, 10 cases (32.3%) had shortness of breath symptoms, 10 cases (32.3%) had fatigue symptoms, 9 cases (29%) had fever symptoms, 4 cases (12.9%) had chest tightness symptoms, and 3 cases (9.7%) had convulsion symptoms. In terms of physical signs, 10 cases (32.3%) had audible vascular murmur, 10 cases (32.3%) had disproportionate limb blood pressure, and 9 cases (29%) had abnormal peripheral vascular pulsation. 3. Laboratory examination: 18 (58.1%) patients had elevated CRP, 19 (61.3%) patients had increased ESR, among them, 15 (48.4%) patients had elevated ESR and CRP at the same time. In terms of etiology, the patients were infected with tuberculosis, Streptococcus, chlamydia, mycoplasma, Epstein Barr virus, herpes simplex virus, adenovirus and cytomegalovirus. 4. Vascular involvement: abdominal aorta involvement was the most common (24 cases, 77.4%), right renal artery(18 cases, 58.1%), carotid artery (14 cases, 45.2%), aortic arch or descending aorta (14 cases, 45.2%), subclavian artery (11 cases, 35.5%), superior mesenteric artery (10 cases, 32.3%), coronary artery (6 cases, 19.4%), limb artery (6 cases, 19.4%), pulmonary artery (4 cases, 12.9%).5. Survival analysis: the patient if LVEF always＜45% or ΔLVED always≥8mm, usually have a poor survival.
Conclusion: Among children, the incidence of TA is significantly higher in girl than that in boys, the most common clinical manifestation is hypertension, the most commonly affected site is abdominal aorta. In the early stages of TA, there may not be hypertension out of proportion to the blood pressure of the limbs, but TA should be paid attention to if the child continues to have fever, accompanied by elevated inflammatory markers such as CRP, ESR, and anti-inflammatory response is not effective. TA with coronary involvement is common. If the heart continues to be affected, it often indicates poor prognosis.

关键字 children, Takayasu arteritis, clinical features, hypertension, abdominal aorta, coronary artery, prognosis

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Hypertrophic cardiomyopathy with restrictive phenotype combined with third-degree AVB: a case report and literature review

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Hypertrophic cardiomyopathy (HCM) is a cardiomyopathy characterized by left ventricular myocardial hypertrophy unexplained by abnormal loading conditions. It is a common type of children cardiomyopathy and an important cause of sudden cardiac death in children and young adults. Recent reports indicated some patients with HCM have severe diastolic abnormalities with restrictive physiology. The clinical manifestations and the progression from typical phenotype HCM to restrictive phenotype is rarely described in detail. In this article, we presented a girl diagnosed HCM which echocardiography (ECHO) was generally normal except for ventricular hypertrophy in recent 3 years. But after performed funnel chest correction surgery, she progressed to heart failure combined with the left and right atrium enlarged obviously, hepatomegaly, severe congestion of systemic circulation, all of these are the manifestations of restrictive cardiomyopathy (RCM). The girl had atrioventricular block (AVB) before admission, it was further aggravated during hospitalization. She could not tolerate the low heart rate (HR) and installed a temporary pacemaker, and finally installed a permanent pacemaker. This case can serve as a warning for clinicians when providing cares for HCM patients with RCM phenotype, it often indicates a serious condition and a poor prognosis.

关键字 Hypertrophic cardiomyopathy (HCM), Restrictive cardiomyopathy (RCM), atrioventricular block (AVB), children cardiomyopathy

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Correlation analysis of ACA/D Dimer/CRP and CAL/multiple organ damage in children with Kawasaki disease

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Aim：Kawasaki Disease (KD) is a systemic vasculitis with unknown etiology. In addition to cardiovascular system involvement, it can also have other multiple organs involved. This study is to investigate the correlation between anti-cardiolipin antibody (ACA)/D Dimer/C reactive protein (CRP) and coronary artery lesions (CAL)/multiple organ lesions in children with KD.
Methods: Retrospective analysis of 284 KD/IKD patients from May 2015 to April 2016. Among them, 175 were males (61.6%), with average age of 2 years and 5 months old. Patients were divided into ACA+ group and ACA- group, elevated D Dimer group (DDE) and normal D Dimer group (DDN), and coronary artery injury (CAL) group and non-coronary artery injury (NCAL) group.
Results: ACA was most likely tested positive in younger KD children ($p<0.05$). ACA+ and hypoproteinemia were correlated with CAL, thrombocytosis, and granulocytopenia ($p<0.05$-0.01). Levels of cTnI and CK in CAL group were significantly higher than those in NCAL group ($p<0.05$). CAL was more frequently detected in younger patients and patients with prolonged fever, later IVIG treatment, and elevated CRP over 100mg/L; but there was no statistically significant difference (all $p>0.05$). In KD with DDE group, the incidence of granulopenia, thrombocytosis, myocardial damage, cholestasis, hypoproteinemia, and aseptic urethritis was significantly higher than that in KD with DDN group ($p<0.05$-0.01). However, elevated D Dimer was not associated with CAL. CRP elevation was highly correlated with D Dimer, but not with CAL.
Conclusion: Higher incidence of CAL and myocardial damage was detected in ACA+ and hypoproteinemia groups of KD patients. The younger patients and hypoproteinemia had increased CAL detected. The higher D Dimer was associated with increased multiple organs injuries. CRP was closely correlated with D Dimer, but not correlated with ACA and CAL.

关键字 anticardiolipin antibody; D Dimer; Kawasaki disease;

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The Complementary Relationship Between Echocardiography and Multi-Slice Spiral CT Coronary Angiography in the Diagnosis of Coronary Artery Thrombosis in Children With Kawasaki Disease

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Aim: To compare the diagnostic values by using transthoracic echocardiography (ECHO) and multi-slice spiral CT coronary angiography (CTCA) for identifying coronary artery thrombosis in children with Kawasaki disease (KD).
Methods: Total 97 KD children with coronary artery dilation complications in our hospital from June 2012 to December 2020 were included in the study. CTCA and ECHO were performed after over 1 month of illness.
Results: Coronary artery thrombosis was found in 14 out of 97 patients. Among them, 10 were identified as positive by CTCA, 9 were identified as positive by ECHO, and 5 were identified as positive by both CTCA and ECHO.
Conclusion: Both CTCA and ECHO can be used to diagnose coronary artery thrombosis. ECHO has advantage in identifying low-density thrombus, and CTCA is better for the clot in distal coronary artery. They can complement each other.

关键字 Echocardiography; Multi-Slice Spiral CT Coronary Angiography; Coronary Artery Thrombosis; Kawasaki Disease;

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Copy number variation analysis reveals novel candidate genes in patients with congenital heart disease and extracardiac malformation

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Abstract
Objectives
Extracardiac malformations (ECM) are commonly observed in patients with congenital heart diseases (CHD), affecting the perioperative management and contributing to the progression of the disease. However, the genetic etiology underlying these complex CHD remains elusive.
Methods
We detected copy number variations (CNV) in 103 sporadic CHD patients with ECM by chromosomal microarray (CMA) analysis and conducted a set of gene prioritization processes using ToppGene and self-organizing feature map (SOM) analyses.
Results
Two gross chromosomal aberrations and sixty CNV were detected in our cohort. The overall diagnostic yield of CMA testing for CHD patients with ECM was 15.53% and 21.36% when considering pathogenic CNV and aneuploidy or pathogenic, likely pathogenic CNV and aneuploidy as a positive finding, respectively. The classification of ECM in this cohort indicated that the neurodevelopmental malformations (NDM) were the most frequent comorbidity, followed by craniofacial defects and urinary system diseases. Therefore, we collected the genes in CNV detected in CHD patients with NDM, and through in-depth gene prioritization processes, NDE1, TERT, and COL22A1 were identified as candidate genes for CHD and ECM, especially NDM.
Conclusions
Our study indicated the importance of CMA as the first-tier genetic tool in clarifying the mechanisms underlying CHD with ECM. Since NDM was the most common ECM and a significantly higher CMA diagnostic yield was discovered in CHD patients with NDM, we focused on the CNV detected in CHD patients with NDM and combined ToppGene analysis with SOM clustering for gene prioritization. Our gene prioritization processes may provide a new sight for disease causal genes identification.

关键字 copy number variation; congenital heart disease; extracardiac malformation

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A novel variant c.2262+3A>T of the SCN5A gene resulted in tron retentionassociated with Brugada syndrome

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Objective Voltage-gated sodium channel Nav1.5 encoded by the SCN5A gene plays crucial roles in cardiac electrophysiology. Previous genetic studies have shown that mutations in SCN5A are associated with multiple inherited cardiac arrhythmias. Here, we investigated the molecular defect in five Chinese children with clinical manifestations of arrhythmias.
Methods Gene variations were screened using whole-exome sequencing and validated by direct Sanger sequencing. A mini-gene assay and reverse transcription PCR (RT-PCR) were performed to confirm the effects of splice variants in vitro. Western blot analysis was carried out to determine whether the c.2262+3A>T variant produced a truncated protein.
Results By genetic analysis, we identified five heterozygous SCN5A variants in Chinese children with arrhythmias included two novel variants. In particular, the splice variant c.2262+3A>T, predicted to activate a new cryptic splice donor site, was identified by insilico analysis. The variant retained 79 bp at the 5′ end of intron 14 in the mature mRNA. Furthermore, the mutant transcript created a premature stop codon at 818 amino acids (p.(R818*)), which produced a truncated protein.
Conclusion We reported 5 variants in SNC5A with early onset inherited arrhythmia disorders, which expands the mutation spectrum of the SCN5A gene in Chinese population. We verified the pathogenic effect of splicing variant c.2262+3A>T which disturbed the normal mRNA splicing and caused a truncated protein, suggesting that splice variants play an important role in the molecular basis of early onset incessant ventricular tachycardias, and careful molecular profiling of these patients will be essential for future effective personalized treatment options.

关键字 Brugada syndrome，SCN5A，splice variant

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Risk factors and predictive models for coronary artery lesions in Kawasaki disease independent of antibiotic use in Chinese children

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Objectives: To study the impact of antibiotics used in Kawasaki disease (KD) with coronary artery lesions (CAL) and identify independent risk factors, construct a predictive system.
Methodology: This study reviewed the records of 287 KD patients between the years 2016 and 2020. Patients were grouped by their outcome, CAL group, and a no-coronary artery lesions (NCAL) group and stratified by the use of antibiotics. We collected clinical and laboratory data before the intravenous immunoglobulin (IVIG) treatment.
Results: The two groups of KD patients with and without CAL were compared. The results showed that immature granular cells percentage (odds ratio [OR]=1.310, 95% confidence interval [CI]: 1.048-1.638, p=0.018), total protein (OR=2.573, 95% CI: 1.191-1.5.561, p=0.016) and chlorine (OR=1.325, 95% CI:1.038-1.629, p=0.024) were found to be independent risks factors for CAL. After excluding the cases with antibiotic usage, immature granular cells percentage (OR=1.417, 95%CI: 1.103-1.819, p=0.006), total protein (OR=3.193, 95% CI: 1.182-8.624, p=0.022) were considered the independent risk factors for CAL. After eliminating the interference of antibiotics, the predictive system showed better fit and predictive ability, ROC curve showed that the AUC value and sensitivity and specificity of predicting KD with CAL were 0.780, 60.0%, and 86.8%, respectively.
Conclusion: Immature granular cells percentage and total protein were independent risks for CAL in KD without antibiotics use history. The predictive system (included immature granular cells percentage, total protein, albumin, globulin, chlorine) can be used to predict the occurrence of KD with CAL in Chinese children. The use of antibiotics affected the physiological indicators of KD patients.

关键字 Kawasaki disease, coronary artery lesions, risk factors, antibiotics, predictive system

分类：2. Cardiology 心脏心血管
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Trends of serum folate and homocysteine during early pregnancy and offspring congenital heart disease

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Background: Whether trends of maternal serum folate (SF) and homocysteine (HCY) differ between mothers of offspring with congenital heart disease (CHD) and those of offspring without CHD during early pregnancy is still unknown. This study, for the first time, demonstrated the trends of SF and HCY levels between these two groups during early pregnancy and further explored the optimal time-window and warning levels for screening at-risk mothers with CHD offspring.

Methods: This is a prognostic study with participants from the Shanghai PreConception Cohort (SPCC) and a Shanghai local maternal and child health hospital, between Jan 2017 and Apr 2018. We included pregnancies with SF and HCY data within 16 weeks of gestation. Data on clinical confirmed offspring CHD were extracted from the Information Management System for Neonatal CHD Screening. To balance the measurement error among different hospitals, we used z-scores of the SF and HCY levels calculated by means and standard deviations (SD) rather than the raw data. Linear mixed effect models were used to demonstrate the trends of SF and HCY z-scores during early pregnancy for mothers without CHD offspring and for those of with CHD offspring. Logistic regression models and restricted cubic spline (RCS) analysis were used to estimate the associations between maternal SF and HCY level and CHD offspring.

Result: A total of 24,540 pregnancies were included (10,763 from SPCC and 13,993 from the local hospital), with 199 (0.81%) CHD offspring were obtained. The median gestational week of blood sample collection was 14.6 (interquartile range: 11.7-15.4) week. Among mothers, the z-scores of the SF and HCY were almost unchanged. The SF trends of mothers with CHD offspring did not differ significantly from mothers without CHD offspring throughout the early pregnancy ($P = 0.083$). Similar trends were observed for HCY before 13th week, whereas higher HCY was observed for mothers with CHD offspring after 14th weeks ($P < 0.001$). The mother with CHD offspring respectively had 0.54 SD, 2.54 SD 1.44 SD higher HCY than the controls in 14th week, 15th week, above 16th week. For this subgroup above 14th week, the odds ratio of CHD per HCY level (umol/L) was 1.89 (95% CI: 1.56-2.30), and such an association is likely to be nonlinear based on our RCS analysis (P for non-liner < 0.001).

Conclusions: The SF trends of mothers with CHD offspring did not differ significantly from those without CHD offspring throughout the early pregnancy, whereas higher HCY was observed for mothers with CHD offspring after 14th weeks and present a non-linear relation with CHD offspring. The higher HCY level after 14th week should be considered as a prognosis factor to identification of mothers of CHD offspring ahead.

关键字 Key word: Offspring congenital heart disease, Serum folate, Homocysteine

分类：2. Cardiology 心脏心血管
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Maternal hypertensive disorder of pregnancy and offspring early-onset cardiovascular disease in childhood, adolescence, and young adulthood: A national population-based cohort study

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Background
The prevalence of cardiovascular disease (CVD) has been increasing in children, adolescents, and young adults in recent decades. Exposure to adverse intrauterine environment in fetal life may contribute to the elevated risk of early-onset CVD. Many have shown that maternal hypertensive disorders of pregnancy (HDP) are associated with increased risks of congenital heart disease, high blood pressure, increased BMI, and systemic vascular dysfunction in offspring. However, empirical evidence on the association between prenatal exposure to maternal HDP and early-onset CVD in childhood and adolescence remains limited.
Methods
We conducted a population-based cohort study using Danish national health registers, including 2 491 340 individuals born in Denmark from 1977 to 2018. Follow-up started at birth and ended at the first diagnosis of CVD, emigration, death, or 31 December 2018, whichever came first. Exposure of maternal HDP was categorized as pre-eclampsia or eclampsia (n= 68 387), gestational hypertension (n=18 603), and pre-gestational hypertension (n= 15 062). Outcome was the diagnosis of early-onset CVD from birth to young adulthood (up to 40 years old). We performed Cox proportional hazards regression to evaluate the associations and whether the association differed by maternal history of CVD or diabetes before childbirth. We further assessed the association by timing of onset and severity of pre-eclampsia.
Results
We found that exposure to maternal HDP was associated with a 23% increased risk of early-onset CVD (hazard ratio [HR]: 1.23; 95% CI = 1.19 to 1.26). The HRs for pre-eclampsia or eclampsia, gestational hypertension, and pre-gestational hypertension were 1.22(95% CI, 1.18 to 1.26), 1.25(95% CI, 1.17 to 1.34), and 1.28(95% CI, 1.15 to 1.42), respectively. We also observed increased risks for type-specific CVDs, in particular for hypertensive disease (HR, 2.11; 95% CI, 1.96 to 2.27) and myocardial infarction (HR, 1.49; 95% CI, 1.12 to 1.98). Strong associations were found among offspring of mothers with CVD history (HR, 1.67; 95% CI, 1.41 to 1.98) or comorbid diabetes (HR, 1.56; 95% CI, 1.34 to 1.83). When considering timing of onset and severity of pre-eclampsia on offspring CVD, the strongest association was observed for early-onset and severe pre-eclampsia (HR, 1.48, 95% CI, 1.30 to 1.67).
Conclusions
Offspring born to mothers with HDP, especially mothers with CVD or diabetes history, were at increased risks of overall and certain type-specific early-onset CVDs in their first decades of life. These findings suggest that better management of maternal hypertension, particularly in early phase of pregnancy, may contribute to the reduction of CVD burden in childhood, adolescence, and probably beyond. Further

research is warranted to better understand the mechanisms underlying the relationship between maternal HDP and early-onset CVD in offspring.

关键字 Hypertensive disorders of pregnancy, cardiovascular disease, childhood, adolescence

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Identification of novel single nucleotide variants with potential of mediating malfunction of microRNA in congenital heart disease

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Congenital heart defects (CHDs) represent the most common human birth defects. Our previous study indicates the malfunction of microRNAs (miRNAs) in cardiac neural crest cells, which contribute to the development of the heart and the connected great vessels, is likely linked to the pathogenesis of human CHDs. In this study, we attempt to further search for causative single nucleotide variants (SNVs) from CHD patients that mediating the mis-regulating of miRNAs on their downstream target genes in the pathogenesis of CHDs. As a result, a total of 2925 3’UTR SNVs were detected from a CHD cohort. In parallel, we profiled the expression of miRNAs in cardiac neural crest cells and found 201 expressed miRNAs. A combined analysis with these data further identified three 3’UTR SNVs, including NFATC1 c.*654C>T; FGFRL1 c.*414C>T and CTNNB1 c.*729_*730insT, which result in the malfunction of miRNA-mediated gene regulation. The dysregulations were further validated experimentally. Therefore, our study indicates that miRNA-mediated gene dysregulation in cardiac NCCs could be an important etiology of congenital heart disease, which could lead to a new direction of diagnostic and therapeutic investigation on congenital heart disease.

关键字 congenital heart defect; micoRNA, neural crest cells, single nucleotide variant, posttranscriptional regulation

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Clinical characteristics and follow-up study of rare mitochondrial cardiomyopathy in Chinese children

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[Object]
Mitochondrial cardiomyopathy (MCM) is an important cause of cardiomyopathy in children, which can be caused by either mutations in the mtDNA or in nuclear genes coding for mitochondrial proteins. Due to the heterogeneity of clinical manifestations, it is difficult to early diagnose. The association between prognosis and the genetic background of MCM has yet to be fully elucidated. Here, we investigated the Clinical characteristics and follow-up study of MCM in Chinese children.
[Method] By whole-exome and mitochondrial sequencing, we identified 8 individuals from 215 children with cardiomyopathy as MCM. In addition to the basic agents for cardiomyopathy, mitochondrial cocktail therapy was subsequently applied including CoQ10 (200 mg/day), riboflavin (400 mg/day), and L-carnitine (1-2 g/day). The follow-up time ranged from 1 year to 4 years.
[Result]
The age of onset in the 8 MCMs ranged from 6 months to 13 years old. Clinical features included elevated Plasma lactate (8/8) , fatigability (7/8) , mild intellectual disability(4/8), arrhythmia(2/8), epilepsy(2/8). 3 individuals had DCM, 4 had HCM in combination with phenotype of DCM, 1 had LVNC. According to the genetic testing, one individual had mtDNA mutation, and six individuals had mutations in ntDNA gene. Individual-1 and Individual-2 were both had two heterozygous rare variants in GTPBP3 (MIM 608536), but had different cardiac phenotypes. Individual-1 was a 3-year-old girl who presented with fatigability, the combination of HCM and DCM. Individual-2 was 13-year-old boy who presented with DCM, atrial septal defect, arrhythmia (VT and AF). A new homozygous mutation in DNAJC19 that causes early onset dilated cardiomyopathy syndrome (DCMA) was identified in a 1-year-old boy (Individual-3), whose old brother had the same clinical manifestation and sudden death at 3 years old. Individual-3’s LVEF and LVED nearly resumed normal, unfortunately, he had sudden death at 3 years old. Individual-4 was a 13-year-old girl who presented with serious fatigability, the combination of HCM and DCM, and WPW syndrome, she was confirmed to carry two heterozygous rare variants in MTO1. Individual-5 was 1-year-old boy who presented with mild intellectual disability, epilepsy, and DCM with HCM, a mtDNA mutation (M-TRNI, 4300A>G, >99.85%) was identified in this boy. Individual-6 was a 7-month-old girl who presented with HCM, she was confirmed to carry two heterozygous rare variants in ELAC2. She did not take mitochondrial cocktail therapy. During the fellow-up, her exercise tolerance gradually deteriorated. Individual-7 was a 3-year-old boy who presented with heart murmur, markedly elevated Plasma lactate, DCM and HCM. He was confirmed to carry two heterozygous rare variants in ACAD9. Individual-8 was a 8-month old bay, presented with coma, cyanosis, metabolic acidosis and hyperlactatemia, HCM and DCM, he was confirmed to carry Homozygous mutations in MIPEP gene, his condition was worsened and died after 2 months. During the fellow-up, 6 of 8 MCMs were treated with mitochondrial cocktail therapy, and they all had improvements of exercise and cardiac function.
[Conclusion]

In conclusion, the possibility of mitochondrial cardiomyopathy should be considered in case of that a children with cardiomyopathy presents with the combination of HCM and DCM, Hyperlactacidemia, developmental retardation, neuromuscular dysfunction and other multi-system dysfunction. Genetic testing is strong recommended. In addition to basic agents for cardiomyopathy, mitochondrial cocktail therapy may be benefit.

关键字 Mitochondrial cardiomyopathy，mtDNA，gene mutation

分类：2. Cardiology 心脏心血管
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Exercise test assisted diagnosis of small heart syndrome in children: a case

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ABSTRACT: Objecharacteristics, research status and treatment of small heart syndrome in children. Methods：The clinical data of one child with small heart syndrome were retrospectively analyzed. Results：The child, girl, was 11 years old with clinical manifestations of intermittent anterior cardiac pain. A chest radiograph showed a cardiothoracic ratio of 0.4. A color Doppler ultrasound showed that the room diameter of each room was the normal low value for children of the same age. Dyspnea, the electrocardiogram showed a horizontal shift of the ST segment, and a depression of 0.13 mV at 80 ms after point J for 1.2 min. The exercise test was positive. Conclusion：This report suggests that exercise testing can be used as a new method to assist the diagnosis of small heart syndrome.

关键字 KEYWORDS: small heart syndrome; cardiothoracic ratio; exercise test

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Gestational leucylation suppresses embryonic TBX5 signal and causes congenital heart disease

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Background: Dysregulated maternal nutrition, such as vitamin deficiencies and excessive levels of glucose and fatty acids, increases the risk for congenital heart disease (CHD) in the offspring. However, the association between maternal amino-acids levels and CHD is unclear. Accordingly, in this study, we aimed to determine whether dysregulated levels of the amino acid leucine were involved in the development of CHD.
Methods: We used nuclear magnetic resonance spectrometry (NMRS) to profile amino-acid concentrations in plasma samples obtained from 202 and 212 pregnant women bearing CHD and non-CHD children, respectively. The teratogenic effects of amino acids on heart development were validated in high-amino acid-diet fed and transgenic mouse models. The mechanism driving leucine-associated CHD was investigated using conventional methods including tandem affinity purification and co-immunoprecipitation.
Results: Increased leucine levels in human maternal plasma during first, second, and third trimester were associated with elevated risk for CHD in the offspring. High levels of maternal leucine increased embryonic lysine-leucylation (K-Leu), catalyzed by leucyl-tRNA synthetase (LARS). LARS preferentially bound to and catalyzed K-Leu modification of T-box transcription factor TBX5, whereas SIRT3 removed K-leu from TBX5. Reversible leucylation retained TBX5 in the cytoplasm and inhibited TBX5 transcriptional activity, thereby increasing the risk for CHD. Increasing embryonic K-Leu levels through either maternal high-leucine-diet fed or knockout of Sirt3caused CHD in the offspring in our mouse models. Targeting K-Leu using leucine analogue leucinol inhibited LARS activity, reversed TBX 5 K-Leu modification, and decreased the occurrence of CHD in our high-leucine-diet fed mice.
Conclusions: Our results showed thatincreased maternal amino-acid levels increased the risk for CHD in the offspring by inhibiting embryonic TBX5 signaling, indicatedthat leucylation exerted teratogenic effects during embryonic heart development and may be an intervening target of CHDs

关键字 gestational leucylation; TBX5; congenital heart disease;

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Research progress of bronchopulmonary dysplasia associated with pulmonary hypertension

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Recently, with the rapid development of neonatal care technology, the rate of premature infants survival has been significantly improved. The incidence of brochopulmonary dysplasia(BPD) has greatly increased every year. BPD is a common clinical chronic lung disease[1]. Due to the abnormal development of pulmonary vascular bed and pulmonary vascular remodeling of BPD patients, it is easy to be complicated with pulmonary hypertension[2] , especially in children with moderate or severe bronchopulmonary dysplasia[3]. The clinical symptoms of BPD-associated pulmonary hypertension are hidden. It is well recognized that PH-BPD and BPD with chronic respiratory failure share similar risk factors and over-lapping symptoms, making differentiation challenging. and it is often irreversible, with a high rate of disability and mortality, so it has become one of the intractable diseases in recent years[4].At present, The etiology of the disease is not clear. In clinical, the effectiveness and benefits of treatments are still controversial. Standardized, unified measures for preventing and controlling the disease are still lack. This paper reviews progress on the diagnosis and treatment of BPD with PH in order to improve the understanding, to provide references for the diagnosis and treatment of the disease.

关键字 Bronchopulmonary Dysplasia; Pulmonary Hypertension; Diagnosis; Treatment

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Values of Tenascin-C in Predicting Susceptibilities of IVIG Responsiveness and Coronary Artery Lesions in Kawasaki Disease

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Objective: To explore the value of tenascin-C, a novel serum biomarker, in predicting susceptibilities of intravenous immune globulin(IVIG) responsiveness and coronary artery lesions (CALs) in patients with Kawasaki disease (KD), and to establish novel models for predicting IVIG non-responsiveness and CALs in combination with other widely used clinical parameters.
Methods: Serum samples were enrolled before the initial IVIG treatment in Kawasaki patients admitted to Children's Hospital of Fudan University from October 2018 to November 2020. We measured tenascin-C level by enzyme-linked immunosorbent assay. Clinical features and laboratory parameters were collected, including gender, age, time interval between the onset of the disease and the administration of initial IVIG, white blood count, neutrophil percentage, platelet count, hematocrit value, C-reactive protein, alanine aminotransferase, aspartate transaminase, total bilirubin, serum sodium and Echocardiography data. Based on the response to the initial IVIG treatment, the subjects were divided into IVIG-sensitive group and IVIG-non-responsive group. Student's t test, Mann-Whitney U test or chi-square test were performed between the IVIG-sensitive and IVIG-non-responsive group, as well as non-CALs and CALs group . Multivariable logistic regression was performed to analyze the independent risk factors for IVIG non-responsiveness and CALs. Combined with tenascin-C and other independent risk factors, new predictive models of IVIG non-responsiveness and CALs were established.
Results: A total of 312 KD patients were enrolled, among whom 51 received IVIG therapy before admission to our center. For the remaining 261 patients with initial IVIG after admission, the median serum tenascin-C level of the IVIG-sensitive group (n = 210) and the IVIG-non-responsive group (n = 51) was 12.38 IU/L and 15.44 IU/L, respectively (P < 0.001). Multivariable logistic regression analysis showed that the independent risk factors for IVIG non-responsiveness were elevated tenascin-C, increased total bilirubin, decreased albumin and serum sodium. A new prediction model of IVIG non-responsiveness was established according to the regression coefficient, including tenascin-C ≥13.47IU/L, 1 point; Serum sodium ≤133mmol/L, 2 points; Total bilirubin ≥7.45μmmol/L, 1 point; Albumin ≤32.3g/L, 1 point. The total score was 5, and ≥2 points was defined as a high risk for IVIG non-responsiveness. The sensitivity and specificity of this novel simple scoring model were 78.4% and 73.8%, respectively.
Among the 261 KD patients with the initial IVIG after admission, median level of serum tenascin-C without CALs (n = 219) and with CALs (n = 42) was 12.10IU/L and 19.76IU/L, respectively (P < 0.001). Multivariable logistic regression analysis showed that the independent risk factors for CALs were elevated tenascin-C, delayed

IVIG administration and increased platelet count. According to the regression coefficient, a new predicting model of CALs was established, including tenascin-C ≥16.86IU/L, 3 points; the time interval between the onset and the administration of IVIG ≥6 days, 1 point; Platelet count ≥450×10^9/L, 2 points. The total score was 6 points, and ≥3 points was classified as a high risk of CALs. The sensitivity and specificity of this simple scoring model were 83.3% and 74.0%, respectively. Conclusion: The elevated serum level of tenascin-C is an independent risk factor for both IVIG non-responsiveness and CALs. Tenascin-C can be complementary to widely used clinical parameters in establishing the novel predicting models. Compared with some commonly applied models, our new prediction models showed more sensitivity for IVIG non-responsiveness, combined with both more sensitivity and specificity for CALs.
关键字 Kawasaki disease; Tenascin-C; IVIG non-responsiveness; coronary artery lesions; prediction

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Baseline left ventricular ejection fraction associated with symptom improvements in both children and adolescents with postural tachycardia syndrome under metoprolol therapy

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Background: Postural tachycardia syndrome (POTS) is a common childhood disease that seriously affects the patient's physical and mental health. This study aimed to investigate whether pre-treatment baseline left ventricular ejection fraction (LVEF) and left ventricular fractional shortening (LVFS) values were associated with symptom improvement after metoprolol therapy for children and adolescents with POTS.
Methods: This retrospective study evaluated 51 children and adolescents with POTS who received metoprolol therapy at the Peking University First Hospital between November 2010 and July 2019. All patients had completed a standing test or basic head-up tilt test and cardiac echocardiography before treatment. Treatment response was evaluated 3 months after starting metoprolol therapy. The pre-treatment baseline LVEF and LVFS values were evaluated for correlations with decreases in the symptom score after treatment (ΔSS). Multivariable analysis was performed using factors with a P value of <0.100 in the univariate analyses and the demographic characteristics.
Results: A comparison of responders and non-responders revealed no significant differences in demographic, hemodynamic characteristics, and urine specific gravity (all $P > 0.050$). However, responders had significantly higher baseline LVEF (71.09% ± 4.44% *vs.* 67.17% ± 4.88%, t = -2.789, $P = 0.008$) and LVFS values (40.00 [38.00, 42.00]% *vs.* 36.79% ± 4.11%, Z = -2.542, $P = 0.010$) than the non-responders. The baseline LVEF and LVFS were positively correlated with ΔSS (r = 0.378, $P = 0.006$; r = 0.363, $P = 0.009$), respectively. Logistic regression analysis revealed that LVEF was independently associated with the response to metoprolol therapy in children and adolescents with POTS (odds ratio: 1.201, 95% confidence interval: 1.039-1.387, $P = 0.013$).
Conclusions: Pre-treatment baseline LVEF was associated with symptom improvement after metoprolol treatment for children and adolescents with POTS.

关键字 Children; Left ventricular ejection fraction; Left ventricular fractional shortening; Metoprolol; Postural tachycardia syndrome

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Periconceptional maternal red blood cell folate and the risk of offspring congenital heart disease: nested case-control and Mendelian randomization studies

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Importance: Periconceptional maternal folate is critical to fetal heart development. Prior epidemiological studies have produced inconsistent results on the association of folic acid supplementation or serum folate with offspring congenital heart disease (CHD) risk. Evidence is lacking on periconceptional maternal red blood cell (RBC) folate.

Objective: To quantify the association between periconceptional maternal RBC folate and offspring CHD risk.

Design: A nested case-control study within the prospective Shanghai PreConception Cohort (March 2016-December 2020), a one-sample Mendelian randomization (MR) study, and a two-sample MR study using published summarized data.

Setting: Twenty-eight maternity institutions in 10 districts of Shanghai City, China.

Participants: A total of 122 mothers of offspring with CHD were identified from 19,817 women with pregnancy outcomes and were matched with 488 mothers of healthy offspring on maternal age, enrollment period, and participating site. One-sample MR used data with 115 CHD cases, and two-sample MR used data with 4653 cases from a meta-analysis of candidate genetic association studies.

Exposure: Maternal RBC folate measured one year before and up to 14 weeks of conception.

Main outcome and measures: Odds ratio of offspring CHD. The maternal MTHFR C677T variant was used as the genetic instrument in the MR analyses.

Results Mothers in both groups had a mean (IQR) age of 30.0 (28.0-33.0). In multivariable-adjusted conditional logistic regression models, per 100 nmol/L increment in maternal RBC folate was associated with a 7% reduced offspring CHD risk (Odds Ratio [OR], 0.93; 95% CI, 0.88 to 0.99). Restricted cubic spline analyses indicated that CHD risk decreased with higher RBC folate in a linear manner and continued past the 906 nmol/L threshold. One-sample MR analysis adjusted for maternal age showed a nominal reduced risk in offspring CHD (OR, 0.87; 95% CI, 0.73 to 1.02). This became evident in the two-sample MR analysis (OR = 0.73; 95% CI, 0.64 to 0.84).

Conclusions and Relevance: Higher maternal RBC folate is associated with lower offspring CHD risk in a dose-response pattern. Biologically optimal levels may be higher than the currently recommend 906 nmol/L, and this needs to be further clarified in future studies.

关键字 red blood cell folate; congenital heart disease; causality; nested case-control study; Mendelian randomization

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Efficacy and Safety of Infliximab Therapy for Children with Kawasaki Disease

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Objective: To evaluate the efficacy and safety of infliximab (IFX) therapy for children with Kawasaki disease.

Methods: Children with Kawasaki disease, who were admitted to Children's Hospital of Fudan University from January 2014 to April 2021 and had a history of IFX administration, were enrolled in this retrospective study. We summarized the indications for IFX administration, response rate, drug adverse events and the outcome of coronary artery aneurysms (CAA).

Results: A total of 68 patients were enrolled, including 52 males (76%) and 16 females (24%). Age of onset was 2.1 years (47 days to 10.5 years). IFX was administered to: (1) 35 children (51%) with persist fever who did not respond to intravenous immunoglobulin (IVIG) or steroids, of whom 28 (41%) developed CAA before IFX therapy; (2) 32 children (47%) with continuous progression of CAA; (3) 1 child with persistent arthritis. Median age at IFX administration was 2.1 years (2 months to 10.6 years). In all cases, IFX were administered as additional treatment (median number of days of illness: 21 days [7~59 days]), with 29% as second-line treatment, 29% as third-line treatment, and 41% as fourth- (or more) line treatment. Fourteen children (21%) did not respond to IFX, and received additional treatment mainly including steroids, additional IVIG and cyclophosphamide. Nosocomial infections (11 cases, 16%) that occurred after IFX administration included respiratory, digestive, and urinary tract infections, and thrush. One case had Calmette-Guérin bacillus-related adverse reactions. All of these adverse events, which may be related to IFX treatment, were cured successfully. Sixty-one children were followed up for 6 months (2~79 months). CAA was not observed in 7 children both before and after IFX treatment. CAA occurred in 54 children before IFX treatment, regressed in 23 (43%) children and returned to normal in 10 children during follow-up.

Conclusions: IFX is an effective and safe treatment option for Kawasaki disease children who are refractory to IVIG or steroids treatment, or with continuous progression of CAA.

关键字 Kawasaki disease; Infliximab; Coronary artery aneurysm

分类：2. Cardiology 心脏心血管
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Unrecognized Congenital Heart Disease in School-age Children in Rural China: A Population-Based Echocardiographic Screening Study

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Background Unrecognized congenital heart disease (CHD) in childhood continues to be a significant public health burden in developing countries, particularly in rural areas. Accurate estimates of the prevalence of unrecognized CHD in school-age children could contribute to quantifying unmet health needs for diagnosis and treatment. Completed as part of the Health Poverty Alleviation Project in China, we aimed to provide the first estimate of real-world prevalence of unrecognized CHD in this population from a representative rural area in China.

Methods We did a population-based echocardiographic screening study of 21 861 children aged 5 to 18 years in one town and four townships (99·2% of all school-age children) in Luchun County between December 1, 2019 and November 31, 2020. The diagnosis, severity, and indications for treatment of CHD were ascertained by a team of trained pediatric cardiologists. The primary outcome was the prevalence of unrecognized CHD, defined as CHD diagnosed for the first time during the screening. Risk factors for unrecognized CHD were examined by multivariable logistic regression analyses.

Results A total of 285 CHD cases were identified, providing a prevalence of 13·0 per 1000 (95% confidence interval 11·6 to 14·6). Among them, 252 (88·4%) were unrecognized CHD cases, yielding a prevalence of 11·5 per 1000 (10·2 to 13·0). With the addition of three recognized but unrepaired severe CHD, the prevalence of unrepaired CHD was 11·7 per 1000 (10·3 to 13·2). Mild, moderate, and severe lesions accounted for 27·4%, 60·7%, and 11·9% of the unrecognized CHD, with the most common one being atrial septal defect (63·1%). Higher body mass index z-score (odds ratio 1·46, 95% CI 1·04-2·04), high-poverty area (2·34, 1·01-5·45), poor household (4·16, 1·66-10·40), and mild or moderate CHD (vs severe CHD: 3·96, 1·31-12·01 and 4·87, 1·86-12·75, respectively) were significantly associated with unrecognized CHD.

Conclusion The high prevalence of unrecognized CHD, mainly composed of moderate and severe cases, indicates that missed diagnosis of clinically significant CHD is a major issue in rural China. It is crucial to increase the awareness of unrecognized CHD and disseminate standardized educational and healthcare services in rural areas to reduce the disease burden.

关键字 congenital heart disease; echocardiographic screening; school-age children; population-based study; rural areas

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Identification and validation of cardiac regulatory elements of NKX2-5, ACTC1 and TNNI1

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Objective: Regulatory elements (REs) are essential to heart development, and related variations are associated with congenital heart disease (CHD). Enhancer is one of the most important category of REs and regulates the spatio-temporal expression of target genes. NKX2-5, ACTC1 and TNNI1 are CHD-related key genes. We aimed to identify cardiac enhancers of these CHD-related genes to facilitate the study of the etiology of CHD.

Methods: The Chromatin immunoprecipitation and sequencing (ChIP-seq) data identified in human and mouse heart samples were collected from Cistrome DB; enhancer-related histones were H3K4me1, H3K4me3 and H3K27ac. Evolutionary Conserved Region (ECR) Browser was used to perform conservation analysis of human (hg19) and zebrafish (zv9) genomes to screen ECRs. ChIP-seq data were mapped to hg19 by using LiftOver. Candidate enhancers were screened in a region covering NKX2-5, ACTC1, TNNI1 with 100 kb upstream and downstream of them. Putative transcription factor binding sites (TFBSs) were analyzed using JASPAR and PROMO and the core region of enhancer was analyzed according to the distribution of cardiac transcription factors (TFs). The enhancer activity was identified using zebrafish embryos and the luciferase reporter assay. Co-localization analysis was performed to compare the heart-specific fluorescence expression of *Tg(myl7: mCherry)* (a transgenic line with cardiomyocyte-specific red fluorescence driven by the promoter of *myl7*) and enhancer mediated transgenic zebrafish line in this study. A correlation analysis between the enhancer and TFs was performed via TF overexpression and TFBS mutation experiments.

Results:

Quantification and score of cardiac enhancers based on ChIP-seq analysis

A total of 49 heart-related and enhancer-associated ChIP-seq datasets were collected in this study. The score of every candidate enhancer sequence was calculated according to the frequency of this sequence in these datasets (score range: 0-1000. A higher score indicated that the candidate enhancer has a stronger cardiac correlation).

In vitro and in vivo identification of enhancer activity

ECRs and enhancer sequence with scores greater than 700 were termed candidate enhancers in this study. We screened 11 NKX2-5-related, 7 ACTC1-related and only one *tnni1b* (zebrafish homologous gene of TNNI1) related candidate enhancers. In vitro and in vivo identification of enhancer activity showed that 3 NKX2-5-related, 2 ACTC1-related and 1 *tnni1b*-related enhancers drove the luciferase expression in cardiomyocytes, while only *tnni1b*-related enhancer (a 183 bp ECR located ~84 kb upstream of *tnni1b*, termed tnni1b-z183) was capable of driving specific GFP expression in zebrafish hearts.

An 87 bp cardiac-specific enhancer has positive correlations with the cardiac TFs including NKX2-5 and JUN

The core region of this 183 bp ECR was only 87 bp (termed tnni1b-z183-d2), which drove the specific GFP expression near the atrioventricular junction. The GFP pattern

in zebrafish embryos was similar to the expression profiles of *tnni1b*. In addition, a correlation analysis showed that the enhancer activity of tnni1b-z183-d2 increased when NKX2-5 (p = 0.0006) or JUN (p < 0.0001) was overexpressed, but significantly decreased when the TFBSs of NKX2-5 (p < 0.0001) or JUN (p = 0.0018) were mutated.

Conclusions: (1) There were a lot of functional enhancers near the CHD-related genes NKX2-5, ACTC1 and TNNI1. (2) An 87 bp cardiac-specific enhancer located 84 kb upstream of *tnni1b* was positively correlated with the cardiac TFs including NKX2-5 and JUN. (3) The GFP expression mediated by tnni1b-z183-d2 is a valuable tool for marking the domain around the atrioventricular junction, which means that the related transgenic zebrafish line is helpful for cardiovascular research. (4) Our method is of great significance to guide the study of functional REs related to cardiac development or CHD, especially the effect of long-range variations of genes on CHD.

关键字 congenital heart disease; ChIP-seq; big data analysis; genome wide; regulatory region

分类：2. Cardiology 心脏心血管
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The Experimental Study on Human FGFBP2 Homologous Gene Regulating Zebrafish Embryonic Heart Development

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OBJECTIVE: To identify the human FGFBP2 homologous gene subtype, which is closely related to heart development in zebrafish, and analyze it’s temporal and spatial expression patterns. Construct the gene knockout zebrafish model then observe its effects on heart development. And preliminarily investigate its regulatory effect on BMP / Nodal signal pathway.
Methods: Bioinformatics analysis showed that zebrafish genome had two human FGFBP2 homologous genes fgfb2a and fgfbp2b. The fgfbp2b mutant zebrafish line (ZKO431a) has normal heart development, and the cardiac phenotype induced by suppressing Fgfbp2a protein expression in the fgfbp2b mutant is as same as with the cardiac phenotype obtained by suppressing Fgfbp2a protein expression in normal zebrafish embryos. Therefore, the gene in zebrafish that is homologous to human FGFBP2 and is critical to heart development is fgfbp2a. The temporal and spatial expression profiles of fgfbp2a gene during zebrafish embryonic development were drawn by constructing gene RNA probes and by using the whole embryo in situ hybridization experiment. The fgfbp2a gene knockout zebrafish model was constructed by CRISPR / cas9 technology to observe the heart development. Immunoprecipitation assay was used to detect whether fgfbp2a protein can bind to ligands and receptors of BMP / nodal signaling pathway. In addition, the effect of fgfbp2a gene knockout on the expression of left-2, the target gene of BMP / nodal signaling pathway was detected.
Results: By drawing the spatiotemporal expression profile of fgfbp2a, it was determined that it was expressed in the periphery of the heart tube. The fgfbp2a gene knockout zebrafish model has been successfully constructed by using CRISPR/Cas9 technology. Knockout of fgfbp2a gene can cause the phenotype of the heart with abnormal d left and right axis. The embryonic cardiomyocytes of the control group migrated to the left and front. The fgfbp2a gene knockout embryonic cardiomyocytes cannot migrate to the left and front but gather in the midline to form a ″midline jogging″ heart tube, which is consistent with the reported phenotype of the combined blocking of both the BMP and Nodal signaling pathway. Fgfbp2a protein can bind to BMP2 signal pathway ligand BMP4 and type II receptor ACTRⅡ of BMP / nodal signal pathway. The knockout of fgfbp2a gene resulted in a significant down-regulation of lefty-2 expression and changes in spatial expression patterns.
Conclusion: The gene in zebrafish that is homologous to human FGFBP2 and is critical to heart development is fgfbp2a. Fgfbp2a plays an important role in the development of the left and right axis of the heart, and it may regulate the development of the heart by influencing the BMP/Nodal signaling pathway.

关键字 FGFBP2, heart, zebrafish, BMP signaling, Nodal signaling

分类：2. Cardiology 心脏心血管
1073

CHD-RPanel: generation and validation of a genome-wide CHD Regulatory Panel based on big data analysis

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Objective: The worldwide morbidity of congenital heart disease (CHD) is up to 9.410‰. However, >50% of CHD patients have no diagnosis even after WES analysis, which indicates that many pathogenic variations in the regulatory regions have not been identified or well studied. Chromatin immunoprecipitation and sequencing (ChIP-seq) is one of the most common methods for identifying functional regulatory elements (REs). In this study, we aimed to efficiently quantify important and specific active cardiac REs based on big data analysis, and generate a CHD Regulatory Panel (CHD-RPanel) that will be valuable for genetic screening, diagnosis and research of CHD.

Methods: Big data integration analysis was performed on >500 human and mouse tissue-related ChIP-seq datasets collected from Cistrome DB database. The cardiac importance and specificity of each RE was quantified at the genome-wide single-base level. Based on this, to assess the efficiency of this strategy in screening active cardiac REs, we selected some potential key regions around the heart-related genes (genes that were highly expressed in the heart or associated with cardiac development or CHD) to study their impact on cardiac development and function. The human cardiomyocyte cell line AC16, human liver cell line MIHA, human kidney cell line 293T and luciferase reporter assay were used to identify enhancer activities. An enhancer knock-out cardiomyocyte cell line was generated using CRISPR/Cas9-mediated genome editing. CCK-8 and flow cytometry were used to detect cardiomyocyte proliferation and apoptosis. RNA-seq and qPCR were used to analyze the genes and signaling pathways that were affected by enhancer deletion.

Results:

Generation of a genome-wide CHD-RPanel based on big data analysis

Here, we efficiently identified a large number of functional cardiac REs, which composed a 43 Mb CHD-RPanel. This panel accounted for ~1.5% of the human regulatory region (the heart-important and heart-specific REs accounted for 1.1% and 0.4%, respectively).

Validation of enhancer activity confirmed the efficiency of this CHD-RPanel in identifying active cardiac enhancers.

In this study, we chose 30 heart-important and 22 heart-specific candidate enhancers for functional validations after considering multiple factors including distance from target genes (a total of 328 heart-related genes were included in this study), randomness and diversity. Luciferase assay showed that 50% (15/30) of heart-important enhancers and 27% (6/22) of heart-specific enhancers were capable of increasing the luciferase expression in AC16 cells, and 83% (5/6) of the active heart-specific fragments showed no enhancer activity in the non-heart (control) cell lines (MIHA and 293T).

CRISPR/Cas9-mediated enhancer knock-out had important effects on human cardiomyocytes

To further study the effect of active enhancers on cardiac development and/or function, we knocked out a 1007 bp active heart-important enhancer (termed hmu-27)

that located 27 kb upstream of NOTCH1 in AC16 cells. Compared with wild-type, hmu-27 deletion had important effects on cell proliferation, apoptosis and multiple signaling pathways including Dilated Cardiomyopathy, Hypertrophic Cardiomyopathy, and MAPK signaling pathways.

Conclusions: (1) In this study, we firstly developed an efficient screening and functional analysis strategy for regulatory region studies at the genome-wide level based on big data analysis. (2) We innovatively generated a 43 Mb CHD-RPanel and confirmed the efficiency of this panel in identifying active cardiac enhancers. (3) The CHD-RPanel established in this study is of great significance for cardiovascular research, and also has important application value for the etiology screening and diagnosis of CHD, especially those with no variations in coding regions.

关键字 congenital heart disease; genome-wide; regulatory region; noncoding variations; variations of unknown significance; ChIP-seq

分类：2. Cardiology 心脏心血管
1107

Bayesian Inference and Neural Feedback for Diagnosing Infantile Congenital Heart Disease

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Objects: Congenital heart disease (CHD) is the most common birth defect in infants. Deep learning-based CHD diagnosis networks (CHDNet) have shown astonishing performance, even achieved or exceeded expert level, but the crucial issue of reliability of diagnostic results needs to be resolved, which directly determines whether doctors are willing to use them.
Methods: (1) Acquired a large-scale real-world echocardiogram data of three common congenital heart diseases, including secondary atrial septal defect (ASD) and ventricular septal defect (VSD), patent ductus arteriosus (PDA) for training and validation. (2) Respectively trained three CHD diagnosis networks for three common congenital heart defects using three representative deep networks. (3) Introduced the Bayesian inference to measure the reliability of diagnosis and the neural feedback to improve the reliability of diagnosis. (4) Applied the trained networks on the internal and external test sets and presented experimental results quantitatively and qualitatively.
Results: Totally 470,400 images are acquired from 5,880 echocardiograms records of 12- to 38-month infants who underwent routine clinical care and imaging examination from January 1, 2015, to June 30, 2020 at Children's Hospital of Fudan University. We show how Bayesian inference applies to CHDNet to obtain the reliability of results. Furthermore, to improve the reliability and robustness of diagnosis, inspired by the feedback mechanism in human visual cortex, we devise a computational neural feedback cell that allows CHDNet to feed knowledge from the output layer back to shallow layers and enables it to selectively activate relevant neurons. Using three representative deep models, we demonstrate how reliability obtained by Bayesian inference interprets and quantifies the significant performance difference between internal and external test sets of three common congenital heart defects, and how the devised feedback cell helps CHDNet to maintain high accuracy and reliability, despite the input is severely damaged by noise or CHDNet have been specially enhanced.
Conclusions: Taken together, our results show CHDNet can, in combination with Bayesian inference and neural feedback, achieve better accuracy, higher reliability, and stronger robustness in diagnosing three common congenital heart defects. These two technologies introduced in this work can be easily embedded in existing deep neural network-based diagnosis approaches, thus improving their performance and reliability. We predict that the current explosion of echocardiogram data richness and the ability of CHDNet to dynamically adapt to various CHD cases with neural feedback will release the great clinical potential of CHDNet and make such learning approaches prevalent in clinic.

关键字 CHDNet; ASD; VSD; PDA; Bayesian Inference; Neural Feedback

分类：2. Cardiology 心脏心血管
1122

Comorbidity of chronic fatigue syndrome, postural tachycardia syndrome and narcolepsy with MTHFR mutation in an adolescent: a case report and literature review

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Objective: To review the diagnosis and pathogenesis of CFS in pediatric population, the major progress of the diagnosis and treatment of the complications in this case as well as the latest recommendations in the management of CFS.
Methods: An adolescent case of chronic fatigue syndrome (CFS) accompanied by hyperhomocysteinemia associated with heterozygous mutation of MTHFR gene, postural tachycardia syndrome and narcolepsy was reported. Based on the case, literatures on associated issues were reviewed.
Result: A 16-year-old male adolescent was hospitalized complaining of intermittent dizziness, drowsiness and fatigue for approximately 2 years. The patient had an episode of fever and pharyngalgia lasting nearly 2 weeks and had undergone appendectomy because of acute appendicitis before the presentation of the above symptoms. He suffered from severe dizziness mostly after switching from a supine to an upright posture when he was getting up in the morning. In addition, he felt drowsy and fatigued all day despite a total sleep duration of 14-15 hours per day. The feeling of fatigue was obviously aggravated after exertion or infection. He was unable to focus on his studies and had to withdraw from school for a long time. His physical examination showed no significant abnormalities except for a body mass index of 25.6 kg/m2, indicating overweight. Investigations in the form of a routine complete blood count, a liver and renal function test, serum electrolytes, cortisol circadian rhythm and thyroid function were normal. Meanwhile, his serum homocysteine concentration markedly increased to a maximum value of 86.14 μmol/L (reference range: 6-17 μmol/L). Relevant investigations, including serum folate and vitamin B12, blood amino acid and urinary organic acid analyses, were normal. Family-wide exome sequencing showed complex heterozygous mutations in the MTHFR gene. A serum immunoglobulin assay revealed significantly elevated titers of Epstein-Barr virus (EBV) capsid antigen immunoglobulin (Ig) G (>750 U/ml, reference range: <20 U/ml). No abnormal results were reported in his examinations of Holter monitoring, echocardiography and ambulatory blood pressure monitoring. A standing test showed that his heart rate (HR) increased from 61 beats per minute (bpm) when supine up to 118 bpm during upright as he complained of lightheadedness. Intensive flow-mediated vasodilation (FMD) was confirmed. Repeated magnetic resonance imaging (MRI) of the brain and routine electroencephalogram (EEG) showed no abnormalities. However, the multiple sleep latency test (MSLT) showed that his sleep latency was shorter than 8 minutes, and 3 sleep-onset rapid eye movement (REM) periods (see supplemental material 1) in 5 naps and his Epworth sleepiness scale (ESS) score added up to 19, which indicated an evident sleep disorder. No abnormalities were found in otorhinolaryngologic and ophthalmic examinations.
CFS, also known as myalgic encephalomyelitis (ME) or ME/CFS, can occur at all ages while the diagnosis of CFS was often made at school age and adolescence. It is believed that CFS is a physical disease in nature caused by multiple complex mechanisms that have not been fully understood. Predisposing factors include female, genetic background, etc., and possible triggers of symptoms include infection, vaccination, physical or mental trauma, overfatigue, chronic sleep deprivation and

exposure to poisons or drugs. Orthostatic intolerance is a significant feature of CFS in children and narcolepsy is an important complication that will influence the prognosis. In recent years, the relationships between MTHFR gene polymorphism and CSF began to attract the researchers' attention.
Conclusion: Multiple aspects should be taken into account when treating patients with CFS regarding the complex etiology. Great attention should be paid to CSF in childhood to increase the diagnostic rate and give more comprehensive and effective treatment for children patients.

关键字 chronic fatigue syndrome; postural tachycardia syndrome; narcolepsy; MTHFR mutation

分类：2. Cardiology 心脏心血管
1223

Functional assessment of heart-specific enhancers by integrating ChIP-seq data

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Background: Decades of extensive genetics research have led to a deeper understanding of CHD causation than ever before with the rapid development of genome-wide association studies (GWASs) and massively parallel sequencing. However, nearly 80% of mutations found by whole-genome sequencing (WGS) in the isolated CHDs beyond regions of known CHD genes cannot be appropriately explained. Except for new CHD genes, the majority of putative causative mutations identified with WGS reside in the noncoding region of the genome, which accounts for nearly 95% of the whole genome. Identification and functional annotations of regulatory sequences play a pivotal role in heart development and function.
Methods: In the present study, we creatively integrated 148 ChIP-seq data sets mapping enhancer-associated chromatin marks (H3K4me1, H3K4me3, H3K27ac) in heart tissue and control tissue from mice and humans to identify heart-specific enhancers. Then, this “virtual heart-specific enhancer panel” including approximately predicted putative human enhancer elements was combined and calculated by importance scores. Subsequently, a comparison with the published heart-enhancer catalogs was performed to analyze our method’s efficiency. Finally, functional validation of heart-specific enhancer activity and possible target genes were identified in cultured cells.
Results: A total of 148 data sets was included and divided into six groups according to their species, sources and histone marks. All the profiles downloaded from the Cistrome DB website were analyzed through a uniform processing pipeline based on the human GRCh38/hg38 assembly and the mouse GRCm38/mm10 assembly. To unify all the genome coordinates and genome annotations between different assemblies, we transferred all the downloaded profiles from the original version to the human GRCh37/hg19 assembly using the LiftOver tool. Finally,the size of a 144.6-Mb candidate heart-specific enhancer compendium was generated by integrating the analysis of 148 epigenomic data sets from human and mouse hearts and control tissues.
The size of our present compendium is only about twenty five percent of the published integrated 35 ChIP-seq data from heart (published in the Journal of Nature Communication), indicating that our set is much more heart-specific and has an priority on core regions. Meanwhile, one hundred percent of the reported heart-specific enhancers were overlapped with putative heart-specific enhancers in our catalogue which lays the foundation for subsequent experimental verification. To further validate in vivo enhancer activity, we tested 12 of these sequences around 45 CHD-related genes in cultured cells and revealed that 8 (67%) of them have reproducible heart-specific enhancer activity. A functional analysis demonstrated that the identified human heart-specific enhancer wf1 regulates the FBN1 gene which is involved in heart disease.
Conclusions: Our study provided an integrative analysis pipeline for ChIP-seq data and identified a comprehensive catalog of human heart-specific enhancers for clinical CHD -related studies.

Impact statement:

1. Establishing an efficient way to analyze regulatory regions in CHD is very important.
2. A highly qualified heart-specific enhancer compendium was generated by integrating 148 online ChIP-seq samples.
3. Sixty-seven percent of predicted regulatory sequences have reproducible heart-specific enhancer activity in vivo.
4. Human heart-specific enhancer wf1 regulates the CHD-related FBN1 gene.

关键字 Enhancer; ChIP-seq; Heart; CHD; Integration

分类：2. Cardiology 心脏心血管
1344

Associations of Maternal Gestational Diabetes Mellitus with Alterations in Cardiovascular System in Early Childhood

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Abstract
Objective: The association of maternal gestational diabetes mellitus (GDM) with childhood cardiovascular alterations is not well established. This study was aim to test the hypothesis that prenatal exposure to GDM is associated with vascular and cardiac alterations in early childhood.
Methods: In a population-based prospective cohort among 1,094 mothers and their offspring, GDM was diagnosed according to the International Association of Diabetes and Pregnancy Study Groups criteria. Childhood blood pressure (BP) measurement and echocardiographic examination were performed using standardized methods at 4 years old. The association between maternal GDM and childhood BP and cardiac outcomes was modeled using linear regression. Mediation analysis was conducted to test the potential mediators.
Results: Maternal GDM was associated with higher systolic BP (SBP; β, 1.20; [0.11, 2.28]), lower left ventricular end-diastolic diameter (LVEDD; β, -0.36; [-0.71, -0.01]) and lower end-diastolic volume (EDV; β, -1.46; [-2.75, -0.18]) in offspring at the age of 4 years. After stratification by sex, the association became stronger in male offspring (SBP: β, 1.94; [0.37, 3.51]; LVEDD: β, -0.60; [-1.09, -0.12]; EDV: β, -2.09; [-3.86, -0.31]) and was independent of maternal and child characteristics. However, no significant difference was found in female offspring. Mediation analysis showed the effects on childhood cardiovascular alterations were attributable to the direct effects of maternal GDM mostly.
Conclusion: Our results provide evidence that maternal GDM is associated with offspring cardiovascular adaptations at preschool age. Further studies are needed to replicate our results and find the underlying mechanism of male-predominant cardiovascular alterations.

关键字 gestational diabetes mellitus, blood pressure, cardiovascular alterations, prospective cohort

分类：2. Cardiology 心脏心血管
1409

Atrioventricular Nodal Reentrant Tachycardia and Atrial Flutter Combined Exist Simultaneously in a 1-month-old Infant

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Background:
Transesophageal cardiac electrophysiological study can identify the type of supraventricular tachycardia and may find some special electrophysiological phenomena.

Method:
A 1-month-old female infant was admitted to our hospital for cardiac electrophysiological study because of recurrent pale complexion and supraventricular tachycardia recorded by electrocardiogram (ECG). No obvious abnormalities were found in cardiac physical examination, echocardiography, and routine ECG and 24-hour dynamic ECG. After intravenous injection of Midazolam, the patient was sedated. The 7F esophageal electrode was inserted through the nose, and transesophageal cardiac electrophysiological study was carried out.

Results:
The infant underwent atrial RS2 program stimulation. When the coupling interval reached 70ms, the S2 -R interval was prolonged by 83ms (> 60ms), and then narrow QRS tachycardia with a frequency of 280 beats/min was induced (Figure 1). The retrograde P wave was buried in the QRS complex, and the RP interval in the esophageal lead was 36ms (< 70ms). When RS2 stimulation was continued on the esophageal electrode and the coupling interval was 60ms, the tachycardia turned to atrial flutter (AFL) (Figure 2). The F wave interval in esophageal lead was regular, with a frequency of 480 beats/min. AFL could terminate by itself (Figure 3). Electrophysiological diagnosis: 1. Atrioventricular nodal double pathway conduction phenomenon; 2. Inducing slow-fast AVNRT and AFL.
One atrial premature beat could turn AVNRT into AFL, suggesting that there was a correlation between the two kinds of tachycardia in the infant. The results of electrophysiological study have important value in the follow-up treatment of arrhythmia in the infant. Recently, when the infant will suffer from narrow QRS tachycardia again, if the ventricular rate is 280 beats/min, it is mostly AVNRT; If the ventricular rate is 240 beats/min, high vigilance against AFL should be recognized. In the long run, when the infant would undergo supraventricular tachycardia slow pathway ablation, it is suggested that interventional physician should pay attention to ablation of atrial muscle near coronary sinus ostium to cure AVNRT and AFL at the same time.

Conclusion:
Transesophageal cardiac electrophysiological study is viable, safe and non-invasive, additionally can help to find some important ECG phenomena. It is especially suitable for infants who are temporarily inaccessible to receive radiofrequency ablation.

关键字 transesophageal, electrophysiological, atrioventricular nodal reentrant tachycardia, atrial flutter, infant

分类：2. Cardiology 心脏心血管
1414

Prominent gallbladder enlargement: Kawasaki disease? Or other congenital or acquired gallbladder disease?: A case report.

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Background: Kawasaki disease (KD) is a common systemic vasculitis in childhood, which can result in multiple system damage, but the related distinct gallbladder (GB) enlargement in acute stage is especially rare.
Method: A 5-year-old boy was admitted to the hospital with cervical mass for 8 days, fever for 7 days, abdominal pain and rash for 5 days. The child was diagnosed with KD. After the treatment with high-dose intravenous immunoglobulin (IVIG) (2g/kg), clinical manifestations were relieved except abdominal pain. The enhanced Computed Tomography (CT) showed that the gallbladder (GB) had distinct enlargement, and congenital choledochal cyst was strongly suspected (Figures 1A, 1B, and 2A).
Results: After the child received a large-dose of glucocorticoid treatment, his obviously enlarged gallbladder returned to normal size in the subacute phase (Figure 2B). No abnormality was found in the follow-up of 2 years.
Conclusion: Prominent GB enlargement may emerge in the acute stage of KD. The enlarged GB can recover to normal within subacute stage by standard treatment for KD. Proper diagnosis, thorough differential diagnosis and active anti-inflammatory treatment of KD are crucial to avoid surgery.

关键字 Kawasaki disease, gallbladder, computed tomography, glucocorticoid therapy

分类：2. Cardiology 心脏心血管
1420

Postnatal weight gain on the early blood pressure, left cardiac structure and function in children from birth to 4 years old: a prospective birth cohort in China

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Abstract:
Background: Obesity and rapid postnatal weight gain may be associated with higher cardiovascular diseases risk in from childhood to adult. Our study aimed to explore the relationship between postnatal weight gain and blood pressure, left ventricle structure and function during the early childhood from birth to 4 years old.

Methods: Data of 1043 children from Shanghai Birth cohort were used in this study. Birth weight and height of children were measured after delivery. The blood pressure, echocardiography and anthropometry assessment were evaluated at 4 years of age. The weight gain was calculated as the difference between weight from birth, 2 and 4 years old.

Results: Birth weight was positively associated with the thickness of left ventricle wall in 4 year-old children, but the blood pressure was not significantly associated with it. The correlation between gestational age with blood pressure, left ventricle structure and function was not significant. Postnatal weight gain from birth to 4 years old had positive correlation with blood pressure, left ventricle wall thickness and mass. The weight gain from birth to 2 years old was positively associated with ventricle wall thickness and mass but not significantly associated with blood pressure. But the weight gain from 2 to 4 had more association with blood pressure than left ventricle wall thickness and mass. Children with excessive weight gain from birth to 4 years old [OR=2.3(1.1,4.9)] and 2 to 4 years old [OR=2.4(1.1,5.5)] had increased risk of prehypertension or hypertension, but weight gain from birth to 2 years old was not [OR=1.6(0.8,3.0)].

Conclusions: This study suggested that children with excessive postnatal weight gain was significantly increased the risk of hypertension as early as 4 years old. But the weight gain within the 2 years old, the critical period of catch-up growth might not increase the risk of hypertension.

关键字 Postnatal weight gain, blood pressure, left ventricle structure and function, hypertension

Category: 2. Cardiology 心脏心血管
1459

Modelling X-linked dilated cardiomyopathy due to DMD gene mutation by induced pluripotent stem cells-derived cardiomyocytes

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Abstract Content Background:
X-linked dilated cardiomyopathy (XLDCM) is a serious phenotype of dystrophinopathy caused by mutations of the DMDgene, resulting in dilated cardiomyopathy, rapidly deteriorating heart failure, and thus early death. Unlike Duchenne muscular dystrophy, patients with XLDCM do not have major skeletal muscle weakness. Currently, the only curative treatment is heart transplantation. This research, therefore, aimed to establish an effective platform to model XLDCM and screen potential therapeutic drugs.
Methods:
We generated induced pluripotent stem cells (iPSCs) from a patient with XLDCM with a DMDgene c.31+1G>A intron 1 splice site mutation. Then we differentiated them into cardiomyocytes. Using western blot to test the full-length dystrophin expression and qPCR to measure mRNA expression of dystrophin isoforms. Hypertonic stress was applied to test ATP and cTnI release to characterize the pathological properties. Calcium handling was measured to compare the cardiac function between patient and normal iPSC-CMs. We administered membrane sealant Poloxamer 188 and trichostatin A (TSA), a histone deacetylases inhibitor, on the patient-derived iPSC-CMs, to evaluate the protective effect and underlying mechanism. RNA sequencing was conducted to show the transcriptome profile of normal, patient and TSA-treated patient iPSC-CMs.
Results:
The iPSCs derived from both the patient and normal control expressed pluripotency markers and showed differentiation capacity into the three germ layers in vivoand mutation was confirmed in patient derived iPSC. Cardiac-specific markers were confirmed in theiPSC derived cardiomyocytes (iPSC-CMs). Full length dystrophin (M isoform) was expressed in normal but not in patient derived iPSC-CMs. Deficiencies of dystrophin protein in patient-derived iPSC-CMs were associated with high osmotic fragility with increased ATP and cTnI release and abnormal calcium handling including prolonged time to the peak of the calcium transient and delayed duration of recovery. Poloxamer 188 rescue the abnormal calcium handling calcium handling and could block ATP release from hypotonic stress. TSA treatment significantly reduced the time to peak and decay time of the calcium transient in the patient-derived iPSC-CMs. Expression both of calcium related protein, Na+–Ca2+exchanger 1 (NCX1) and of mRNA expression was significantly higher in patient-derived iPSC-CMs, compared with the normal control, but were downregulated by TSA treatment. RNA-seq data In enriched KEGG pathway analysis, we also identified some common pathways, including the calcium signal pathway, in normal, patient, and TSA-treated patient group. The rescue of the abnormal calcium handling by TSA may be related to the regulation of NCX1 expression.
Conclusion:
This study confirmed that our XLDCM patient-derived iPSC-CMs model provides an effective platform for disease modeling and drug screening.

Methods We generated induced pluripotent stem cells (iPSCs) from a patient with XLDCM with a DMDgene c.31+1G>A intron 1 splice site mutation. Then we differentiated them into cardiomyocytes. Using western blot to test the full-length dystrophin expression and qPCR to measure mRNA expression of dystrophin isoforms. Hypertonic stress was applied to test ATP and cTnI release to characterize the pathological properties. Calcium handling was measured to compare the cardiac function between patient and normal iPSC-CMs. We administered membrane sealant Poloxamer 188 and trichostatin A (TSA), a histone deacetylases inhibitor, on the patient-derived iPSC-CMs, to evaluate the protective effect and underlying mechanism. RNA sequencing was conducted to show the transcriptome profile of normal, patient and TSA-treated patient iPSC-CMs.
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Conclusion This study confirmed that our XLDCM patient-derived iPSC-CMs model provides an effective platform for disease modeling and drug screening.

Key words iPSC; cardiomyocyte; XLDCM;drug screening
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分类：2. Cardiology 心脏心血管
1697

Elabela: a novel biomarker for pulmonary artery hypertension secondary to congenital heart disease

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Abstract
Objectives: The objective of this study was to investigate the changes and significance of Elabela (ELA) levels in patients with pulmonary artery hypertension (PAH) secondary to congenital heart disease (CHD) (PAH-CHD), represented by ventricular septal defect (VSD).
Methods: A total of 80 VSD patients with PAH were recruited in Shanghai Xinhua Hospital from 2018 to 2020. After exclusion of patients complicated with other cardiac malformations, chromosomal abnormalities, or other risk factors for PAH , 46 patients with PAH-VSD and 3 patients with Eisenmenger syndrome were included in our study. All patients were divided into five groups according to the severity of PAH: mild PH (SPAP 30-49 mmHg and/or MPAP 25-40 mmHg), moderate PH (SPAP 50-69 mmHg and/or MPAP 41-54 mmHg), severe PH (SPAP ≥70 mmHg and/or MPAP ≥55 mmHg), Eisenmenger syndrome, and isolated VSD without PH (SPAP < 30mmHg and MPAP < 25mmHg). Peripheral venous blood was collected at admission and echocardiographic examination was conducted for all patients. The plasma ELA concentration was measured using enzyme-linked immunosorbent assay (ELISA).
Results: There was significant difference of ELA concentration among groups (P=0.007). Compared with isolated VSD, patients with PAH-VSD had a lower circulating ELA level (P=0.048). Linear regression models indicated that ELA was significantly associated with SPAP (r=-0.071, P<0.001) and MPAP (r=-0.191, P=0.043). The ability of ELA in predicting reversibility of PAH-VSD was similar to traditional echocardiographic indexes, e.g., PAAT or RV/LV ESD (AUC=0.73).
Conclusions: ELA concentration and severity of PAH-VSD had a significant negative correlation, indicating that ELA might serve as a surrogate marker for the clinical evaluation of PAH in VSD children. Furthermore, ELA might have equivalent value as echocardiographic indexes in predicting reversibility of PAH-VSD.

关键字 Elabela, pulmonary artery hypertension, congenital heart disease

分类：2. Cardiology 心脏心血管
1698

Predisposition to atrioventricular septal defects may be caused by SOX7 variants that impair interaction with GATA4

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Objective: Congenital heart defects (CHD) are the most common birth defect and the leading cause of neonatal mortality. Atrioventricular septal defects (AVSD) are a complicated subtype of congenital heart defects for which the genetic basis is poorly understood. Many studies have demonstrated that the transcription factor SOX7, which can interact with GATA4, plays a pivotal role in cardiovascular development. The critical role of GATA4 in the morphogenesis of the atrioventricular septum implies that SOX7 is potentially involved in AVSD. However, whether SOX7 variants are involved in AVSD pathogenesis needs further exploration.
Methods: In this study, a total of 100 sporadic non-syndromic AVSD Chinese Han patients and 500 matched controls were recruited and SOX7 variants in the patient cohort were screened by targeted sequencing. The identified variants of SOX7 were analyzed by bioinformatics. The mutated plasmids were generated and transfected into HEK293T cells and human umbilical vein endothelial cells, respectively. Function assays including gene transcription level by real-time PCR, protein expression by western blot, subcellular location by immunofluorescence staining, as well as transcription activity analysis by dual luciferase reporter assay were performed to evaluate pathogenicity of nonsynonymous variants of SOX7.
Results: We identified three rare SOX7 variants, c.40C>G, c.542G>A, and c.743C>T, in the patient cohort, but none was found in the control cohort. All mutation sites were found to be highly conserved in mammals. Among the three variants, c.542G>A and c.40C>G were found in ExAC database, but both of their minor allele frequency were lower than 0.005. Notably, Variant c.743C>T was neither found in ExAC nor 1000G. All the three rare variants were likely to be damaging as predicted to be pathogenic in at least 1 program. Compared to the wild-type, these SOX7 variants had increased mRNA expression and decreased protein expression. With the addition of the special protease inhibitor, MG-132, the reduced turnover of P248L and G181E mutants were notably elevated, indicating that certain SOX7 mutations altered protein levels by abnormal protein degradation. The subcellular distribution of SOX7 mutant proteins was similar with those of wild-type proteins, as all of them showed diffuse nuclear localization. Affymetrix human transcriptome array demonstrated that both of SOX7 and GATA4 were highly expressed in human embryonic hearts of Carnegie stage 11-15, which is the critical period of the cardiac septum formation. Immunofluorescence studies revealed that SOX7 and GATA4 were co-localized in the developing atrioventricular cushions, which is the most important embryonic structure for the atrioventricular septum. These results indicated that SOX7 and GATA4 might have joint function in the development of the atrioventricular septum. Moreover, SOX7 overexpression promoted expression of GATA4 in human umbilical vein endothelial cells. A chromatin immunoprecipitation assay revealed that SOX7 could directly bind to the GATA4 promoter and luciferase assays demonstrated that SOX7 activated the GATA4 promoter. The SOX7 variants had impaired transcriptional activity relative to wild-type SOX7. Furthermore, the SOX7 variants altered the ability of GATA4 to regulate its target genes. These results indicated these three rare variants of SOX7 affecting its expression level and interaction with GATA4 contributed to complete AVSD

Conclusion: Our study suggests that the variants of SOX7 are associated with human AVSD and provides novel insight into the genetic etiology of AVSD, which may contribute to the prenatal diagnosis, consultation and treatment for AVSD.

关键字 congenital heart defect, atrioventricular septal defect, SOX7, GATA4

分类：2. Cardiology 心脏心血管
1726

ELA deficiency aggravates DOX-induced acute cardiotoxicity in mice

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Background: ELABELA (ELA) is an early endogenous ligand of apelin receptor (APJ/APLNR), which is a G protein-coupled receptor (GPCR) with seven transmembrane domains. Recent studies have shown that the ELA-APJ system plays an important role in the development and function of the cardiovascular system. **Mehtods and resuts:** In this study, we found that the mRNA expression of ELA was increased in C57BI/6J mouse hearts on the first and second day after doxorubicin (DOX) injection (20mg/kg ip). We also studied the effects of DOX-induced cardiotoxicity in ELA cardiac progenitor cell-specific knockout mice (ELAfl/fl;NKX2.5cre, also name CKO, Conditional ELA deficiency in mouse cardiac progenitor cell). Compared with wild-type mice, CKO mice had a significant decrease in myocardial contractility on Day 2 after DOX administration followed by a decrease in 9-day survival rates. And DOX-induced myocardial injury, and autophagy dysfunction are more pronounced in CKO mice. Rat cardiomyocytes (H9C2 cell line) showed that pretreatment with ELA peptide had a protective effect on DOX-induced cell activity reduction. The protective effect of ELA on DOX-related acute myocardial injury toxicity was eliminated by inhibitors of the AKT pathway.
Conclusion: These results suggest that the deficiency of ELA expression can aggravate the cardiotoxicity induced by DOX, which may be the cause of the decreased protective function of the endogenous ELA-APJ system. Regulation of the ELA-APJ system may bring hope for the treatment of dox-induced cardiotoxicity.

关键字 ELABELA; APJ; PI3K/AKT; doxorubicin; cardio-protective effect

分类：2. Cardiology 心脏心血管
1728

Comparison the copy number variations in pulmonary stenosis and other right ventricular outflow tract obstruction diseases

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Pulmonary stenosis (PS) is one of the most common congenital heart diseases, but the pathogenesis has been unknown. Our study was to determine the contribution of copy number variants (CNVs) in the pathogenesis of PS and further to reveal similarities and differences with other right ventricular outflow tract obstruction (RVOTO) diseases. 174 patients (including 42 PS, 32 PA-IVS, 60 PA-VSD and 40 TOF cases) and 100 controls were determined by whole exome sequencing. We identified seven pathogenic genes (NBPF25P, STAG3L2, LRRC37A, GOLGA8EP, FAM66B, NBPF12, and NBPF10) in PS patients, and found that genes in de novo CNVs of PS patients including IRX4, IRX1, IRX2, FOXQ1, TTN, FOXC1, and MYLK4 were highly related to congenital heart disease. Venn diagrams and GO enrichments indicates that PS & PA-IVS and PA-VSD & TOF likely have similar genetic etiologies. Moreover, some genes could take effect on the degree of severity of the disease. We demonstrated a significantly frequency of rare CNVs in PS patients and provided new insights into understanding for the pathogenesis of right ventricular outflow tract obstruction diseases.

关键字 pulmonary stenosis, copy number variations, right ventricular outflow tract obstruction diseases

In Utero Pediatrics

宫内儿科学

分类：14. In Utero Pediatrics 宫内儿科学
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Tuberous sclerosis complex accompanied with cytomegalovirus intrauterine infection: a case report

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Female, 30 years old, G1P0, she had skin rash and mild fever during early pregnancy, and all were self-limited. During the first trimester, all was normal. But at 23-25 weeks of gestation, the color doppler ultrasonography displayed multiply intracardiac occupations which were considered as cardiac rhabdomyomas. The Pathological examination of fetal cardiac tissue confirmed multiple rhabdomyomas. The 200× whole exome sequencing of the parents' peripheral blood sample and fetal tissues suggested that the fetus had a de novo mutation in gene TSC2. Further deep sequencing of the paternal peripheral blood cell and sperm indicated a low level somatic and germinal mosaicism of the asymptomatic father. At the same time, the cytomegalovirus IgG of the mother was extremely high, thus we also detected the virus in the fetal heart and brain tissue. Cytomegalovirus inclusion bodies were discovered scattered in the brain and heart, IE1 was positive in the heart and brain tissue. All confirmed a combined congenital cytomegalovirus intrauterine infection. Fetal magnetic resonance could be sensitive but with limited specificity in detecting early neurological damage. Mosaicism was more common in sporadic cases of tuberous sclerosis complex, and there may be second-hits caused by infection or other factors which might result in severe neuropathological damage.

关键字 tuberous sclerosis complex, cytomegalovirus, mosaicism

分类：14. In Utero Pediatrics 宫内儿科学
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Severe nausea and vomiting in pregnancy: cognitive and psychiatric problems and brain structure in children

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Background: Two studies have suggested that severe prolonged nausea and vomiting during pregnancy is associated with emotional and behavioral problems in offspring, with smaller sample size and short-term follow-up. Moreover, little information is available on the role of the brain structure in the associations.
Methods: In a US-based cohort, the association was investigated between severe prolonged nausea and vomiting in pregnancy (extending after the second trimester and termed SNVP), psychiatric and cognitive problems, and brain morphology, from the Adolescent Brain Cognitive Development (ABCD) study, from 10,710 children aged 9–11 years. We validated the emotional including psychiatric findings using the Danish National Cohort Study with 2,092,897 participants.
Results: SNVP was significantly associated with emotional and psychiatric problems ($t = 8.89$, Cohen's $d = 0.172$, $p = 6.9 \times 10^{-19}$) and reduced global cognitive performance ($t = -4.34$, $d = -0.085$, $p = 1.4 \times 10^{-5}$) in children. SNVP was associated with low cortical area and volume, especially in the cingulate cortex, precuneus, and superior medial prefrontal cortex. These lower cortical areas and volumes significantly mediated the relation between SNVP and the psychiatric and cognitive problems in children. In the Danish National Cohort, severe nausea and vomiting in pregnancy were significantly associated with increased risks of behavioral and emotional disorders in children (hazard ratio, 1.24; 95% confidence interval, 1.16–1.33).
Conclusions: SNVP is strongly associated with psychiatric and cognitive problems in children, with mediation by brain structure. These associations highlight the clinical importance and potential benefits of the treatment of SNVP, which could reduce the risk of psychiatric disorder in the next generation.

关键字 Nausea and vomiting, Cognitive performance, Psychiatric problems, Cortical structure, Cingulate cortex, Precuneus, Superior medial prefrontal cortex

分类：14. In Utero Pediatrics 宫内儿科学
990

Regulation of placental breast cancer resistance protein in the context of class Ⅰ histone deacetylase: implications for individualized and safe pharmacotherapy by epigenetic regulation during pregnancy

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Background Pharmacotherapy during pregnancy is increasingly common and often inevitable for medical treatment of the mother, the fetus or both. Precise regulation of drugs' transplacental transfer rates is the pivotal point to balance the drug efficacy and toxicity of the mother and fetus. Breast cancer resistance protein (BCRP) is a critical drug efflux transporters by limiting the passage of drugs across the placenta, which is considered as a key molecular gatekeeper to control drugs' transplacental transfer rates. More investigations on the regulation of placental BCRP offer great promise for enabling pronounced progress in individualized and safe pharmacotherapy during pregnancy. Histone deacetylase (HDAC) 1/2/3, core epigenetic enzymes of Class Ⅰ HDACs, are abundantly expressed in trophoblast cells, playing indispensable roles in biological processes. We have recently found that these three HDACs inhibition repressed BCRP expression in placental cells. The purpose of this study was to validate the specific HDAC subtype regulating placental BCRP expression and function in vitro and vivo, illuminating epigenetic implications for individualized and safe pharmacotherapy during pregnancy.

Methods BeWo cells (human placenta choriocarcinoma) were transfected with HDAC1/2/3 specific siRNA. Quantitative real-time qPCR (qRT-PCR), Western-Blot, immunofluorescence and fluorescent dye efflux assay were utilized to evaluate placental BCRP expression, localization, and efflux function after transfection, respectively, identifying the HDAC subtype regulating placental BCRP in vitro. Next, siRNA for the identified HDAC was constructed and intraperitoneally injected to C57BL pregnant mice every 48 h from E7.5 to E15.5. Glyburide, a probe for evaluating placental BCRP efflux functionality, was administered at 100 μg/Kg via the tail vein at E16.5. Animals were sacrificed through cervical dislocation at various times (5-180 min) after drug administration. Expressions and localization of Hdac1/2/3 and Bcrp in placentas were detected by qRT-PCR, Western-blot and immunohistochemistry, respectively; glyburide concentration in maternal plasma and fetal-unit were analyzed by high-performance liquid chromatography/mass spectrometry (HPLC-MS) assay.

Results In vitro, knockdown of HDAC1 expression attenuated placental BCRP mRNA and protein production, without alteration of its intracellular localization, which corresponded with an increase in cellular uptake of the BCRP fluorescent substrate Hoechst 33342. However, no significant differences in BCRP expression and function were noted after HDAC2/3 silencing. Similarly, it was noted that Hdac1 inhibition significantly decreased placental Bcrp expression, with a marked increase of GLB concentrations and area under the concentration-time curve (AUC) in the fetal-units. Particularly, the ratios of fetal unit/maternal plasma GLB concentrations were also significantly elevated following Hdac1 repression.

Conclusion Inhibition of HDAC1 could repress placental BCRP expression and function both in vitro and vivo. Given the discovery of dietary bioactive compounds with the capability of repressing HDAC1, which could be administered safely during pregnancy, HDAC1 might be a novel epigenetic target for individualized and safe pharmacotherapy in the context of controlling drug delivery across the placenta.

关键字 Epigenetic regulation; HDACs ; Breast cancer resistance protein ; Placenta

分类：14. In Utero Pediatrics 宫内儿科学
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The predictive value of the duration of preterm premature rupture of membranes in placental inflammatory lesions and intrauterine

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Background: Premature rupture of membranes (PROM) and chorioamnionitis (CAM) are the main risk factors for premature delivery and infection-related complications in preterm infants. This article aims to explore the relationship between preterm PROM, inflammatory lesions in different parts of the placenta and intrauterine infection complications, to calculte the time cut-off value of PROM predicting for placental inflammatory lesions and infectious complications of preterm infants.
Method: A total of 195 premature infants who were directly transferred to NICU after birth and whose placentas were performed pathological examinations in China-Japan Friendship Hospital within the past 3 years were enrolled. According to the pathological results, 102 cases belonged to the acute inflammation group (including those with only neutrophils infiltration); there were 8 cases presenting acute and chronic inflammatory lesions at the same time; 13 cases were defined as chronic inflammatory lesions, and there were 88 cases in non-inflammatory lesions group. On the basis of histological structure, the acute inflammation group were further divided into 5 subgroups: decidua basalitis/decidulitis, chorionitis, CAM, funisitis, and suspected inflammatory lesions. Then we analyzed the clinical features of mothers and premature infants in each group.
Results: The rate of PROM in the acute inflammation group was significantly higher than that in the non-acute inflammatory lesion group (55.9% vs 29.0%). Then we calculated the cut-off value of PROM duration via receiver operating characteristic (ROC) curve analysis and the results illustrated that when the duration of PROM was ≥14 hrs, the possibility of acute inflammatory lesions in the placenta was greater than that of PROM less than 14 hrs. The histological diagnosis rate of acute inflammatory lesions was higher when the PROM was ≥10.5 hrs. The pathological diagnosis was prone to decidua basalitis/decidulitis with the PROM ≥3.5 hrs; while the PROM ≥7.5 hrs, the placenta were liable to suffer CAM; and ≥56 hrs, the diagnosis of funisitis was more likely. However, the association between the time of PROM and the diagnosis of acute chorionitis or suspected inflammatory lesions showed no significance statistically .
3.5, 7.5, 10.5, 14 and 56 hrs of PROM were used as the cut-off time points to analyze its relationship with intrauterine infection in premature offspring respectively. The results showed that the prevalence of intrauterine infectious diseases in premature neonates whose PROM was ≥7.5 hrs was higher than that of PROM <7.5 hrs, and the specificity of predictive potency was 0.812. Nevertheless, the morbidity of severe intrauterine infectious complications has not been dramatically increased with the time course of PROM over 10.5 hrs, which might be resulted from the usage of antibiotics for maternity before delivery.
We selected 7.5 hrs as the time cut-off value and found that compared with the group of <7.5 hrs (127 cases), preterm infants with PROM ≥7.5 hrs (68 cases) exhibited a growing trend of white blood cell count (13.80±5.29 vs 11.71±5.20), neutrocyte count (7.88±3.52 vs 6.52±3.90), α-L-fucosidase (28.74±10.17 vs 25.37±8.03) and sialic acid levels (25.16± 5.33 vs 22.11±4.63) in serum within 2 hours after birth. However, there were no statistical differences in

gestational age, ventilator supporting time, lymphocyte, platelet, CRP between the two groups.
Conclusions: The longer the duration of the preterm PROM lasts, the closer the placental inflammatory lesions is to the fetus, giving rise to the greater possibility of intra-amniotic infection of the fetus. The duration of PROM ≥7.5 hrs correlates to inflammatory lesions invading the amniotic membrane and has the highest predictive efficiency on intrauterine infectious complications in preterm infants. The preventive treatment of antibiotics for pregnant women with PROM may decrease the incidence of severe infection in preterm infants.

关键字 premature rupture of membranes; preterm infant; placental inflammatory lesions; intrauterine infection; prediction

分类：14. In Utero Pediatrics 宫内儿科学
1404

Changes of dendritic cell and natural killer cell on the cord blood with idiopathic fetal growth restriction

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Objective To investigate the characteristics of dendritic cells (DC) and natural killer
cells (NK) in umbilical cord blood of pregnant patients diagnosed with idiopathic fetal
growth restriction (IFGR).
Methods A prospective study cohort of IFGR patients was established who were in the third trimester (28-36 weeks), with a healthy, pregnant woman cohort selected as controls. Umbilical cord blood was collected.
Results The study included 50 pregnant women in the IFGR group and 50 pregnant women in the healthy, control group. The incidence of SGA in the IFGR group was 52.0%, and the incidence of preterm birth was 18.0%. The incidence of neonatal complications in neonates with live birth in the IFGR group was 12.0%. The birth weight, body length and placental weight of the newborns in the IFGR group were significantly lower than those in the control group ($P < 0.05$). Flow cytometry revealed
no significant difference in the proportion or maturity of DC in umbilical cord blood between IFGR group and control group ($P > 0.05$). The proportion of NK cells in umbilical cord blood of IFGR group was significantly higher than that of normal control group. The proportion of CD56dimCD16+ NK cells was also significantly higher than that of the normal control group ($P < 0.05$), but the expression of NK cell surface killing activator receptor NKG2D and inhibitory receptor NKG2A was not statistically significant ($P > 0.05$).
Conclusion The number and proportion of DC cells in cord blood may not be the key factors affecting the outcomes observed during FGR pregnancies. However, we found the proportion of NK cells in cord blood to be significantly increased, as well as the
ratio of CD56dimCD16+NK to CD56highCD16-NK to be imbalanced, which may be one of the pathogenesis of the pathological pregnancy leading to IFGR.

关键字 Idiopathic fetal growth restriction; Dendritic cells; Natural killer cells

分类：14. In Utero Pediatrics 宫内儿科学
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The association between Autism Spectrum Disorders in offspring and Prenatal antiepileptic drugs use: A Systematic Review and meta-analysis

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The association between Prenatal antiepileptic drugs and Autism Spectrum Disorders risk in offspring: A Systematic Review and meta-analysis

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Objective: To perform a systematic review of the literature of published studies to assess the association between ASDs and fetal exposure to antiepileptic drugs. Methods: A systemic search of MEDLINE, EMBASE, Web of Science and Cochrane Library databases was supplemented by manual searches of references of key retrieved articles. Study quality was evaluated using the Newcastle-Ottawa Scale. The odds ratios (ORs) were used as a measure of the association between fetal exposure to antiepileptic drugs and the risk of offspring autism among studies. The hazard ratios and risk ratios were directly considered as ORs in the pooled analysis. We used a random effects model to calculate the pooled ORs. The I2 statistic (significance level, >50%) and Q statistic (significance level at P< 0.10) were used to assess heterogeneity between studies. Results: The search yielded 4 studies (1321 children) published before 4th April 2021. The studies suggested that valproate (OR 1.76, 95% CI 1.32 to 3.41) and carbamazepine (OR 5.4, 95% CI 1.1 to 26.1) were associated with significantly for developing autism in offspring. However, we found no correlation between oxcarbazepine or lamotrigine use during pregnancy and autism in offspring. Conclusion: Valproate and carbamazepine were associated with the greatest odds of development of autism in offspring compared with control. Counselling is advised for women considering pregnancy to tailor the safest regimen.

关键字 Key words: antiepileptic drugs; autism; offspring; meta-analysis

分类：14. In Utero Pediatrics 宫内儿科学
1706

Protogenin promotes the differentiation of human embryonic stem cells into cardiomyocytes

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PRTG promotes the differentiation of human embryonic stem cells into cardiomyocytes
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Abstract:
Background: Congenital heart disease (CHD), the most common birth defects, affect about 1% of all liveborn infants. Likewise, the incidence of CHD is approximately 0.9% of all live births in China. CHDs include a range of structural and/or functional abnormalities in the heart and/or great vessels resulting from defective embryological events. Single-gene disorders and chromosomal anomalies could be the genetic etiology of CHD, while only approximately 25% of CHDs could be explained according to genetic mutations. Thus, it is important to perfect the pathogenesis of CHD. Protogenin (PRTG) is one kind of transmembrane protein involved in neural development. We found PRTG was also highly expressed in human embryonic heart. This study aims to study whether PRTG plays role in heart development according to inducing the differentiation of human embryonic stem cells (hESCs) into cardiomyocytes (CM) (hESC-to-CM).
Methods: In this study, we collected aborted human embryos and heart tissues during 11CS-15CS (Carnegie Stage). We also observed the expression trend of PRTG during different differential days. In addition, we constructed PRTG-Knockout-hESC (PRTG-KO-hESC) according to Crispr/cas9. By flow cytometry, we tested the differentiation efficiency. Then, we compared differential genes according to RNA-sequence in order to find the mechanism.
Results: We found the mRNA and protein expression level of PRTG were high in human embryos. During hESC-to-CM, PRTG expression level peaked on D5-D6 of differentiation. Compared with hESCs, the pluripotency of PRTG-KO-hESCs was not affected, while the differentiation efficiency decreased significantly (P=0.0001). Based on the results of RNA-sequence, we found some genes associated with heart development were significantly raised in PRTG-KO-hESCs, such as hand1, hand2, gata5, tbx2 and so on. However, protein expression level of these genes was decreased. The specific mechanism still needs our further research.
Conclusion: In this study, the conclusions we can draw so far are: first, PRTG has no effect on pluripotency of hESC; then it can promote the differentiation of hESC into CM; the last, it is associated with heart development but the specific mechanism needs more studies.

关键字 Congenital heart disease; human embryonic stem cells; differentiation of human embryonic stem cells into cardiomyocytes

Early Childhood Development

儿童早期发展

分类：3. Early Childhood Development 儿童早期发展
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Sibling Effect on Psychosocial Well-being and School Readiness in Young Children: A Cross-Sectional Study

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Objective
The current study aims to examine how sibling presence impacts the early childhood development (ECD), including psychosocial well-being and school readiness.
Methods
Data were obtained from a representative sample of kindergarten children (mean age=3.64 years) in Shanghai in 2019 (n=23,917, response rate=99.1%) who were divided into four groups: single-child, younger-child with an elder sibling, elder-child with a younger sibling, twin-child. Psychosocial well-being was measured by the Strengths and Difficulties Questionnaire (SDQ) and school readiness was measured by the early Human Capability Index (eHCI). Propensity score analysis with inverse probability weighting were used to estimate the sibling effect on children’s ECD.
Results
Compared with single-child group, lower risks of being classified as at-risk for psychosocial problem were found in twin-child (OR=0.65, 95% CI: 0.49, 0.88, P=0.004) and younger-child (OR=0.54, 95% CI: 0.49, 0.59, P<.001). Younger-child group were also found with better overall school readiness (β=1.90, 95% CI: 1.55, 2.24, P<.001) than single-child group. Single-child had significantly higher numeracy and literacy skills than children in both younger- and elder-child groups.
Conclusions
Our results revealed that having an elder sibling positively associated with children’s psychosocial well-being and school readiness.

关键字 siblings, child development, mental health, school readiness, Strengths and Difficulties Questionnaire

分类：3. Early Childhood Development 儿童早期发展
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Assessing the Inequality of Early Child Development in China - A Population-Based Study

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Background: As a country with the second largest child population in the world, China has little population-level evidence on who has been left behind in early childhood development (ECD). Knowledge of inequalities in ECD will inform the Chinese government in policies on promoting ECD and guide global-level monitoring on ECD progress.

Methods: Using data from the first wave of ECD surveys conducted in China at the least-developed region, most-developed region, and a megacity (Shanghai) in 2017 and 2018, we measured population-level ECD with early Human Capability Index for a total of 63,559 children aged 36-59 months old. A child was classified as developmentally on track if his/her overall development score was above the 20th percentile of the pooled populations. We measured inequalities in ECD with the absolute inequality in five domains: gender, family income, maternal schooling, residential Hukou, and migrant- or left-behind status. Besides observed inequalities, we used a multilevel logistic regression model to generate adjusted inequalities.

Findings: Children developmentally on track ranges from 71% (95% CI 70 to 72%) in the least-developed region, 82% (95% CI 81 to 83%) in the most-developed region, and 86% (95% CI 85 to 87%) in Shanghai. Significant unadjusted inequalities in ECD were observed in all five dimensions. After controlling for other socioeconomic factors, significant inequalities remained in three dimensions: those living in the poorest families, or with lower maternal schooling, or boys were less likely to be developmentally on track than their counterparts (lower by 10[95% CI 8 to 11]-15[95% CI 13 to 17], 7[95% CI 5 to 10]-10[95% CI 7 to 12], and 5[95% CI 4 to 6]-6[95% CI 5 to 8] percentage points respectively).

Interpretation: Efforts of reducing ECD inequalities in China shall focus primarily on reducing poverty and improving maternal education.

关键字 Early Child Development, China, Inequality

分类：3. Early Childhood Development 儿童早期发展
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Screen Time Trajectory and Early Childhood Development: A Prospective Cohort Study

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Importance: Screen have become an integral part of children’s daily lives. However, the developmental consequence of screen exposure in young children has not been drawn conclusion.
Objective: To investigate the pattern of the screen time trajectory during 6 to 72 months and investigate its effect on cognitive, language, and social-emotional development of children from a prospective birth cohort.
Design, setting, and participants: The prospective birth cohort included 266 children whose mothers were recruited during 34 to 36 gestational weeks between August 2012 and July 2013, from obstetrical department of Renji hospital in Shanghai, China. The children were followed up when they were 6, 9, 12, 18, 24, 36, 48, and 72 months. The onsite assessments were conducted in Shanghai Children’s Medical Center.
Exposure: Screen time of children at 6, 9, 12, 18, 24, 36, 48, and 72 months were reported by mothers.
Main Outcomes and Measures: The cognitive and language development of children was evaluated using the Wechsler Intelligence Scale for Children-the Forth Version at 72 months. The social-emotional development was measured by Strengths and Difficulties Questionnaire which is completed by their mother.
Results: The pattern of children’s screen time trajectory during 6 to 72 months can be classified into three groups: little screen time all along (110 [72.9%]), increased screen time after three years (17 [11.7%]), increased screen time before three years (25 [15.3%]). After correcting for gender, mother’s educational attainment, and family income, the type of temperament at 6 months, compared to children with little screen time all along, children with increased screen time after and before three years were associated with decreased scores of FSIQ (coefficient, -7.41, 95% CI, -12.92 to -1.90; coefficient, -6.51, 95% CI, -12.06 to -0.97) and Working Memory (coefficient, -5.83, 95% CI, -10.43 to -1.23; coefficient, -11.31, 95% CI, -15.34 to -7.28); children with increased screen time before three years was associated with increased scores of Total Difficulties (coefficient, 2.37, 95% CI, 0.35 to 4.36) and Hyperactivity/inattention (coefficient, 1.55, 95% CI, 0.57 to 2.53).
Conclusion and Relevance: Increased screen time during the early stages of life, especially the first three years, predicted worse development of children. Further research is required to identify potential mechanisms.

关键字 Screen time, early childhood development, cohort

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mpact of home confinement due to COVID-19 pandemic on mental health in young children: a natural experiment

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Importance: The outbreak of coronavirus disease in 2019 (COVID-19) has had an enormous impact on people’s health, and profoundly changed our lives and society. However, the impact of pandemic-related home confinement on children’s life and their mental health remains unclear.

Objective: To determine whether COVID-19 related home confinement affects children’s family environment, lifestyles, and mental health.

Design: This study took advantage of a natural experiment by comparing two representative cohorts from the Shanghai Children’s Health, Education and Lifestyle Evaluation, Preschool study from 2016 through 2020. Surveys were conducted at both entry and graduation of kindergarten using the same assessment instruments. Children in unexposed cohort entered kindergarten in 2016, experienced a normal period of kindergarten study and graduated in 2019; those in the exposed cohort entered kindergarten in 2017, were under confinement for five months and graduated in June 2020.

Setting: The study population was selected based on multistage probability cluster sampling and was representative of Shanghai kindergarten children.

Participants: In the non-exposed cohort, 20,324 children responded to the Entry Survey, among whom 16,590 were followed up to graduation. The corresponding numbers in the exposed cohort were 22,136 and 18,409 children, respectively.

Exposure: Home confinement due to COVID-19 pandemic for five months

Main Outcomes and Measures: Parent-reported child mental health, family environments and child lifestyles.

Results: Compared to the non-exposed cohort, the exposed cohort had a significantly increased percentage of children classified as “at-risk for mental health problems”, with an adjusted absolute risk difference of 3.1% (95% Confidence Interval [CI]: 1.9% - 4.4%) for total difficulties measured by the Strength and Difficulty Questionnaire. The effect of the confinement on mental health was larger in children with lower level of parental education. The exposed cohort also had a less favorable family environment, longer media time and sleep duration.

Conclusions and Relevance: In general, the pandemic related home confinement negatively affected children's lives and their mental health. Strategies and actions are urgently needed to strengthen parenting education and mitigate the negative impact.

关键字 新冠疫情，社交隔离，幼儿，心理健康

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The buffering effect of positive parent-child interaction on the association between early life stress and psychosocial well-being in preschool children

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Background: Early life stress (ELS; e.g., exposure to forms of maltreatment, trauma, and violence) could lead to toxic consequences when a child experiences strong, frequent or prolonged adverse events without sufficient buffering protection of adult support. Evidence showed that high frequency of positive parent-child interaction probably could buffer the adverse effect of ELS. However, the evidence supporting the buffering effect of positive parent-child interaction is limited. This study aims to exam the moderating effect of positive parent-child interaction on the correlation between early life stress and psychosocial outcomes by using hair cortisol concentration (HCC) as a biomarker of maltreatment in preschool children.
Methods: A cross-sectional study derived from a population representative longitudinal study was conduct in 2019 in a sample of 17233 children aged 6-7 years. Among the participants, a field survey was designed to assess HCC of 260 children. Parents reported the maltreatment history of their children and completed the Chinese Parent-Child Interaction Scale as well as the Strengths and Difficulties Questionnaire. Hair cortisol concentrations were determined using liquid chromatography tandem mass spectrometry (LC-MS/MS).
Results: Maltreatment is associated with the increased of HCC, and the increased of HCC is associated with the increased risk of psychosocial problems. A higher frequency of positive parent-child interaction had a moderating effect on the correlation between chronic stress exposure (increased of HCC) and total difficulties.
Conclusion: HCC could be an indicator of early life stress in preschool children. A higher frequency of positive parent-child interaction may moderate the association between early life stress and psychosocial problems.

关键字 early life stress, parent-child interaction, psychosocial well-being

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Breastfeeding duration and Psychosocial Development of children at 3 years of Age

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Objective
Breastfeeding is an important early parenting behavior. World Health Organization (WHO) recommends breastfeeding duration up to the age of 2 years or beyond. So far, there has not been sufficient evidence to understand about benefits of breastfeeding beyond 1 year.
As we know, 10-20% of the world’s children and adolescents experience mental health conditions. Researches indicated that a substantial proportion of mental health problems in adults originate early in life. Thus, early intervention focused on nurturing care is important to reduce the risk of mental health problems. Breastfeeding not only provides a meal with needed nutrients for infants, but also is a physical and psychosocial dialogue for building a lasting bond between the mother and her child. Compared with formula fed mothers, both exclusively breastfeeding mothers and mixed feeding mothers spend more emotional care time for their infants. Breastfeeding would be play an important role in children’s psychosocial development. The aim of this study was to investigate the association of prolonged breastfeeding with psychosocial development of children.
Methods
The Shanghai Children’s Health, Education, and Lifestyle Evaluation, Preschool (SCHEDULE-P) study recruited 25,354 children aged 3-4 years old in the junior grade of kindergarten in 2019. Parents of 25,124 children consented to participate in a cross-sectional survey. A sample of 25,106 participants were included with complete data.
Breastfeeding information was collected retrospectively by parent report. Breastfeeding duration was grouped into 6 categories: breasted for <1 month (including mothers who did not breasted), 1 to 5 months, 6 to 11 months, 12 to 17 months, 18 to 23 months and ≥24 months.
Psychosocial status was assessed by parent-reported Strengths and Difficulties Questionnaire (SDQ). To reduce the endogeneity induced by selection bias, we used propensity score analysis with inverse probability of treatment weighting (IPTW) to balance the characteristics among groups, with a set of covariates (age, gender, birth weight, physical health, residential hukou, maternal education, paternal education, father's occupation, mother’s occupation, annual household income, primary caregiver, parental marital status, siblings, parent-child interactions, maternal mental health, maltreatment, participation in early education and level of kindergarten).
Results
Overall, 16.75% (95% CI 16.18, 17.35) children were breastfed for <1 month, 21.70% (95% CI 21.07, 22.35) were breastfed for 1 to 5 months, 35.63% (95% CI 34.88, 36.39) were breastfed for 6 to 11 months, 17.93% (95% CI 17.34, 18.55) were breastfed for 12 to 17 months, 5.35% (95% CI 5.00, 5.71) were breastfed for 18 to 23 months and 2.63% (95% CI 2.39, 2.90) were breastfed for ≥24 months. Mothers with low education level, or with low household incomes were more likely to breastfeed for <1 month (P <0.001). In addition, the mother-child dyad with longer breastfeeding duration presented a higher frequency of parent-child interactions (P <0.001). In IPTW model, the risk of

total difficulties declined progressively with increasing breastfeeding duration. Compared with children who were breastfed for <1 month, the adjusted ORs of total difficulties were 0.98 (0.90-1.08) for 1 to 5 months, 0.82 (0.76-0.90) for 6 to 11 months, 0.85 (0.76-0.93) for 12 to 17 months, 0.79 (0.68-0.92) for 18 to 23 months, and 0.77 (0.63-0.95) for ≥24 months. The similar downward trend was observed in the risk of emotional symptoms.
Conclusions
This study suggests that a longer breastfeeding duration, especially ≥24 months, associated with a reduced risk of psychosocial problems among children aged 3-4 years old.

关键字 breastfeeding duration, psychosocial status, emotional symptoms, propensity score analysis, preschooler

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Individual and parental care environment characteristics underlying resilience in maltreated children

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Background: Maltreated children are at high risk of a range of adverse outcomes, but some of them function resiliently despite their history of adversity. Previous studies have found some factors that improve the resilience, however most of them had low or middle study quality. Moreover, there is lack of population based study that adopt stringent definitions of resilience that require children to show adaptive functioning across multiple domains. The study aimed to find out which individual and child care environment characteristics distinguish resilient from non-resilient children with a population representative sample.
Methods: A retrospective study was conducted in 2019 in a representative sample of 17341 children aged 6 years before their completion of kindergarten in Shanghai, China. Parents reported their children's history of maltreatment, self-regulatory capacity, parent-child interactions, family characteristics, maternal mental health status, overall development status (9 domains including verbal, physical, approaches, numeracy concepts, reading, writing, cultural spiritual, social emotion, perseverance), internalizing and externalizing problems through online platforms. On-site assessment was employed in 993 children to evaluate children's language development and intelligence.
Results: Resilient was defined on the basis of history of maltreatment and children's overall development status, language development and their manifestation of internalizing and externalizing problems. Among all the maltreated children, 24.94%(20.91%-29.46%) were resilient. The results of multiple logistic regression analysis showed that less self-regulatory capacity impairment (aOR=0.92 95%CI:0.89-0.95), only-child (aOR=0.57 95%CI:0.37-0.89) and better maternal mental health (aOR=1.06 95%CI:1.00-1.12) were associated with resilience.
Conclusion: Self-regulation skills, having siblings and better maternal mental health status may contribute to adaptive functioning following maltreatment. Public preventions should focus on the resilient promoting factors in early childhood, for building resilience in maltreated children offers an opportunity to improve the health and wellbeing at early stage of life.

关键字 maltreatment, resilience, psychosocial well-being, cognitive function

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Does provision of meals in early education contribute to catch-up growth among stunted children in Lao PDR?

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Abstract Content Stunting, being too short for one's age, is the result of chronic or recurrent undernutrition. Approximately 150 million children under five experience stunting and associated cognitive impairments throughout the life course. Historically, the negative impacts of stunting have been thought to be irreversible after two years of age. However, there is dispute as to whether children who are stunted before age two have the potential to "catch-up" in height to their non-stunted peers, and if so, if these children also show cognitive catch up.
The Early Childhood Education (ECE) Project, financed by the World Bank, supported expansion of quality ECE services with the objective of improving the development of children aged 3-5 years in disadvantaged communities throughout Northern Lao PDR. Three different community-based interventions were implemented, the impact of which were evaluated through three pragmatic clustered randomised control trials.
Separate to the ECE project, school meals were delivered by the World Food Program in early childhood education and schools in selected villages throughout Northern Lao PDR. Although provision of school meals was not included in the study design, data collected provide opportunity to contribute to the debate around both physical and cognitive catch-up growth. Evidence pertaining to this debate has the potential to inform early development and education strategies internationally.
Methods Participants include 4,948 children aged 2-4 years, living in 376 villages across 5 provinces in Northern Lao PDR. Children were first assessed for stunting between November 2015 and March 2016 and were followed through to approximately two years later in November and December 2017 at age 4-6 years when their height and weight was measured again.
Stunting was calculated based on the World Health Organisation (WHO) Child Growth Standards. Z-scores were calculated for each child's height and age compared to the WHO height for age curves. Children who had a z-score more than 2 standard deviations below the curve were classified as stunted. Provision of school meals at the village level was collated from information provided by the World Food Program, who implements meal provision. Receipt of school meals at the individual level was also collected via caregiver report.
Analyses explored the prevalence of stunting at baseline and follow up among the overall sample and according to children's demographic characteristics. Stunting prevalence over time according to school meal provision was examined to assess the relationship between provision of meals and catch-up growth over time.
Results Approximately half of all children were stunted at baseline. Prevalence of stunting reduced by 8.4% at follow up, approximately one year later. When stratified by age, we found that stunting was most prevalent among 4-year-olds at baseline (55.7%), however, this age group also saw the greatest reduction in stunting at follow up; 12%, compared to approximately 6% for children aged 2 and 3 years. Overall, boys were slightly more likely to be stunted compared to girls, and a greater reduction in stunting at follow-up was observed for girls relative to boys (12.9% and 10.2%, respectively). This suggests that girls were slightly less likely to be stunted and more likely to show catch-up growth. Children who were living in more

socioeconomically disadvantaged household were more likely to be stunted than those in more advantaged households. There was a reduction in stunting at follow up among children across socioeconomic groups, however the more socioeconomically advantaged children saw a much larger reduction (18.4%) than disadvantaged children (9%). School meals were provided by the World Food Program in 61% of villages, however only 39% of caregivers reported their child having a school meal in the previous week at follow-up. Regardless of caregiver report, children living in villages with school meals provided were significantly less likely to be stunted (39.6%) than those in villages without school meal provision (46.8%). This suggests a positive relationship between school meal provision and a reduction in stunting or catch-up growth. Availability and receipt of school meals was much more likely for those in more socioeconomically advantaged groups, leaving a vulnerable population of disadvantaged children who were more likely to be stunted and less likely to receive support in the form of a school meal.

Conclusion Preliminary findings indicate that provision of school meals may help to reduce the prevalence of stunting among children over 2 years. Results have spurred further research to explore if there is a causal relationship between meals provided in an early education setting and catch-up growth. This includes analysis of longitudinal data from Indonesia, Lao PDR, and China, currently underway, using causal modelling techniques that have not before been applied in developmental science to determine the impact of early childhood education services, with and without meal provision, on cognitive development. Future research will seek to develop and implement a model of effective and sustainable food provision in early childhood education that can be transferable to other food insecure contexts. If evidenced, results will be a paradigm shift that significantly widens the scope for intervention among stunted children.

Key words Stunting; undernutrition; early childhood education; nutrition intervention
Reference Not applicable.

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Gender Specificity and Local Socioeconomic Influence on Association of GHR fl/d3 Polymorphism with Growth and Metabolism in Children and Adolescents

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Abstract

Objective: Growth hormone receptor (GHR) mediates the majority of growth hormone biological actions and plays a major role in the postnatal linear growth and metabolic activity during childhood and adolescence. In humans, there are two isoforms of recognized GHR transcripts, full-length GHR (GHR fl) and exon 3-deleted GHR (GHR d3). This study was aimed to evaluate whether GHR fl/d3 polymorphism contributes to the inter-individual variability of growth, metabolism and hypertension in heathy children and adolescents.

Methods: A total of 4730 students aged 6-16 years from Yixing and Suqian city in China were included in this cross-sectional study. Height and BMI were transformed to z-score corresponding to age and gender. Normal BP group was defined as both systolic blood pressure (SBP) and diastolic blood pressure (DBP) less than 90th percentile; average SBP and/or DBP at least 90th, but less than 95th, and/or SBP ≥120 or DBP ≥80 mmHg regardless of age, gender and height was divided into pre-hypertension group; The hypertension group was identified as the average SBP and/or DBP persistently above 95th percentile, and/or SBP ≥140 or DBP ≥90 mmHg regardless of age, gender and height. Peripheral total cholesterol (TC), triglyceride (TG) and glucose (GLU) concentrations in serum were measured. The values of 90th percentile of TC, TG and GLU were calculated to classify the students into normal group and relative high-level group in the association analysis. Multivariate logistic regression model was used to estimate the associations of GHR fl/d3 polymorphism with height z-score levels (reference group: -1≤ height z-score<1 group), obesity (reference group: normal weight group) and hypertension (reference group: normotensive group), while binary logistic regression model was applied in the analysis of GHR fl/d3 polymorphism with metabolic traits using additive (fl/fl vs. fl/d3 vs. d3/d3), dominant (fl/fl+fl/d3 vs. d3/d3) and recessive (fl/fl vs. fl/d3+d3/d3) model. Odds ratio (OR) and 95% confidence interval (CI) were calculated to quantify these associations. Stratification analysis by region were conducted to explore the modification of socioeconomic levels on the associations of GHR fl/d3 polymorphism with childhood height, BMI, metabolic traits and hypertension. Interaction between GHR fl/d3 and gender polymorphism on hypertension risk was investigated.

Results: GHR d3 allele was inversely associated with of overweight, but positively associated with increased TC and TG levels (OR [95% CI] for overweight: 0.754[0.593-0.959], P=0.021; for TC: 0.744[0.614-0.902], P=0.003; for TG: 0.812[0.654-0.998], P=0.047). GHR d3 allele were associated with decreased odds of pre-hypertension in boys (OR [95% CI]=0.791[0.645-0.971], P=0.025), but predisposed higher odds of pre-

hypertension and hypertension in girls (ORs [95% CIs]: 1.379[1.106-1.719], P=0.004; 1.240[1.013-1.519], P=0.037). Interaction of GHR f1/d3 polymorphism with gender contributed to increased odds of pre-hypertension and hypertension (interactive ORs [95% CIs]: 1.735 [1.214-2.481], P=0.003; 1.509 [1.092-2.086], P=0.013). Stratification analysis by region showed that GHR d3 variation was associated with low BMI levels in Suqian boys (the OR [95% CI] of additive model was 1.323 [1.034-1.693], P=0.026). Compared with GHR f1/f1 genotype, the presence of GHR d3 allele was associated with reduced odds of overweight in Suqian girls (OR [95% CI] for the dominant model was 0.456 [0.209-0.996], P=0.049). The fitted tendencies of BMI levels among different GHR f1/d3 genotype carriers with age were differently fluctuated between Yixing and Suqian city.
Conclusion: GHR f1/d3 polymorphism is significantly related with growth, metabolism, and hypertension in children and adolescents with the gender specificity, suggesting that genetic effect of GHR f1/d3 may be modified by the local socioeconomic levels.

关键字 Gender specificity, GHR-f1/d3 polymorphism, Growth hormone receptor, Metabolism, Socioeconomic levels

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Age-related changes in Static and dynamic standing balance of 3-6-year-old Children

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Objective: Standing balance is an important component of physical fitness. It is the foundation for maintaining basic life and completing multiple motor skills. Children aged 3-6 are the sensitive period of Brain Development, body growth and basic motor skills, as well as a critical period for the development of posture and balance control. At present, there is no unified method to detect the static and dynamic standing balance in child worldwide. Previous studies are focused on the age-related changes of school-age children, static balance and exercise intervention effects.There are few researches on the 3-6 years old child, dynamic balance and the discrimination between different static and dynamic detection methods.

Methods: Ninety 3-6-year-old children were recruited and divided into three age groups, with half male and half female in each age group. A 3 × 2 (age × sex) two-factor experimental design was used for 14 standing balance tests. Adopting WII balance board (WBB) (Nintendo, Kyoto, Japan) to collected the time-frequency indexes of 8 static stance balance cop (area, path length and time) including single-leg, tandem, double-leg together and double-leg apart stance during eyes open/closed. Dynamic balance tasks were adopted by beam walking, modified beam walking(30 cm from the ground), y balance, walking on tiptoe, forward jump landing (DPSI-AP)and lateral jump landing (DPSI-ML).the static and dynamic balance ability is investigated by the test indexes. Multiple factor variance analysis was used to investigate the age-related changes of age and sex factors on the standing balance ability of subjects under different balance detection methods. The ANOVA was used to investigate the degree of differentiation of different balance ability test methods

Results: (1) Age has significant effect on 3-6 years old child on static standing balance of single-leg ($p<0.001$), tandem ($p<0.001$), double-leg together with eyes open and closed, which is decrease of COP parameters (sway path length and sway duration) with age. (2) Age has significant effect on 3-6 years old child of all detection of dynamic standing balance (except tiptoe walking: walking time), which shows that the dynamic standing balance ability was increased with age. (3) Age and sex had non-interaction on the static and dynamic standing balance ability of 3-6 years old child. ($p>0.05$) (4) Due to the development period, there are individual difference. but the standing balance ability was increased with age. (5) single-leg and tandem stance; modified beam walking and y balance test can better detect the static and dynamic standing balance ability of 3-6 years old child. Compared with static state, the detection of dynamic may be a better detection method.

Conclusions: The static and dynamic standing balance ability of 3-6 years old child shows special age and sex characteristics. testing and developing the balance ability of preschooler is beneficial to the development of early sports and the sustainable development of future sports. The measurement of dynamic balance ability may be a more effective detection method. Measurement of dynamic balancing ability may be a more effective method.

关键字 Preschooler; Age-Related Changes Static Balance; Dynamic Balance; Standing Balance Ability; Detection Method

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The association of caregivers' hand hygiene and developmental delay in children aged 0~35 months in poor rural China: A cross-sectional study using propensity score matching analysis

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Objectives: This study aimed to examine the association between caregiver's handwashing practices and early childhood development (ECD), where limited evidences are available.
Study design: A community-based cross-sectional survey was conducted among children under 3 years in two poor rural counties of China in 2016.
Methods: Self-reported handwashing practices (no handwashing, handwashing without soap, handwashing with soap) of caregivers at five key times (before food preparation, meal, feeding the child, after defecation and disposal of child faeces), and other factors related to ECD were collected by a household questionnaire. The Chinese version of Age and Stages Questionnaire - third version was used to identify children with suspected developmental delay (SDD). With logistic regression and propensity score matching analysis to adjust covariates and control for confounders, we explored whether caregivers' handwashing with soap was associated with decreased child SDD.
Results: A total of 1,057 children under 3 years were enrolled, with 17.7% with SDD. 852 caregivers washed hands at all the five key times (225 with soap and 627 with water only). Among children of caregivers washing hands at all the five key times, children whose caregivers washed hands with soap had lower risk of SDD (14.4% vs. 23.6%, P=0.002; adjusted OR: 0.6 [95%CI: 0.4 to 1.0]), compared to children whose caregivers washed hands with water only. After propensity score matching, 196 pairs of children were matched, and the difference in SDD prevalence between the two groups was still statistically significant (P<0.001).
Conclusion: Caregivers' handwashing with soap at the key times is significantly associated with improved ECD. The hygiene promotion should be addressed in ECD interventions.

关键字 Handwashing; Caregiver; Early Childhood Development

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Socioeconomic gradient in very young child development: evidence from China based on Ages and Stages Questionnaire (the third edition)

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Objectives: To investigate socio-economic differentials in early childhood developmental performance for children between the ages of 1 to 37 months, in urban, rural and poor rural area, using the Ages and Stages Questionnaires(ASQ) - the third edition in China.
Study design: Data of two cross-sectional studies were used in this analysis. A cross-sectional study using a stratified cluster sampling method was conducted in six administrative regions of the mainland China following the population structure of 2010 national population census in the period of 2011-2012. Another cross-sectional study was conducted in two provinces in two regions, from south and north China, to collect data in poor rural areas in 2013. 83 villages in six poor rural counties of the two provinces were randomly chosen from the national poverty battlefield county list. Respectively, 1,707, 1,691, and 2,937 children from urban, rural and poor rural areas, who were younger than 37 months old, were included in this study.
Methods: Domain- and age-specific developmental delay among different regions were compared to investigate the differentials in early development in China. Multivariable regression analysis was conducted to explore the association of interested socio-economic variables and ASQ performance using the dataset from the poor rural area.
Results: Notable regional disparities across all developmental domains were identified. The overall prevalence in suspected development delay in poor rural, rural and urban was 32.21%, 18.86% and 12.42%, respectively. The biggest disparity between poor rural and urban was observed in fine motor and problem-solving domain. Increased risks of SDD were found in the poorest socio-economic groups in poor rural area (OR: 1.72 [95%CI: 1.28 to 2.31] for the poorest vs. richest; OR: 1.95[95%CI: 1.24-3.06 for the illiterate vs. the high school & above) after controlling for child age, sex, caregiver’s age, sex and ethnicity.
Conclusions: This study is among the first attempt to document the socio-economic disparities in early childhood development in China, using ASQ data from urban, rural and poor rural samples. Results suggested that programs providing supports to children in poor rural areas are urgently needed to attenuate the negative effects of poverty, so as to ensure every child fulfills his/her development potential.

关键字 Socioeconomic gradient, Early childhood development, Age and Stages Questionnaire

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Effects of community-based nurturing care interventions on child growth and hemoglobin status

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Background: This study aims to investigate the effects of a 2-year community-based nurturing care interventions on child growth and hemoglobin status among children left behind in poor rural area of China.
Methods: A 2-year community-based nurturing care interventions comprising of responsive care education and practices, feeding counseling and daily supplementation of Ying Yang Bao(YYB) were conducted in four in four poverty-stricken counties in China. A quasi-experimental design was applied, with data collection before and after in both intervention and comparison areas. Hemoglobin level and anthropometric status was assessed among 1173 left-behind children aged 6-35 months at baseline and 1254 in the final survey following the standard anthropometric and hemoglobin testing procedures. Multiple imputation methods were used for missing values with proportion range 10~22%. A difference-in-difference regression model was applied to estimate the intervention effect on the child height/length, weight, hemoglobin status, as well as on the child stunting, underweight, wasting, and anaemia. Regression analysis was conducted to estimate the association between interventions, YYB intake and growth outcomes.
Results: Enrollment in the programme was associated with significant increase in weight-for-age z score (WAZ) (0.31; P=0.035) and lower risk of child malnutrition (aOR:0.41; 95%CI: 0.19, 0.89) in the children above 24months after controlling for child sex, age, birthweight, diarrheal, caregivers' age, sex, education, and household wealth index. However, no effect was found for height-for-age z score (HAZ), weight-for-length z score (WHZ), hemoglobin level, stunting, underweight, wasting and anaemia indicators, as well as for left-behind children under 24months. Stratified by birthweight, it was found that nurturing care interventions were associated with a reduced risk of stunting (aOR:0.18, P=0.031) among the left-behind children with birthweight lower than -1SD. But no effect was found for underweight, wasting, malnutrition and anaemia prevalence, as well as for left-behind children with birthweight above -1SD. We also found frequent center-based responsive care interventions(≥1 per week) and home visits more than once a month were associated with higher regular use of YYB(aOR: 2.05; 95%CI:1.36,3.09 for centers; aOR: 2.22; 95%CI: 1.62, 3.05 for home visits). While regular YYB consumption was linked with improved HAZ(0.26; 95%CI:0.07,0.44), WAZ score(0.18; 95%CI: 0.02,0.33) and lower risk of stunting(aOR: 0.49; 95%CI: 0.19, 0.68).
Conclusions: Integrated early childhood care and nutrition interventions was associated with improved nutrition status in left-behind children, and effects of the program on child growth should consider intervention density, duration and the birthweight status.

关键字 nurturing care, nutrition, child growth

Category: 3. Early Childhood Development 儿童早期发展
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Barriers to effective parental investment in early language development among peri-urban households in China: A mixed methods study

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Abstract Content Parental investment in the early home language environment is a key input in the development of language and cognitive skills. Studies in Western settings have found differences in parental investment in the home language environment can predict disparities in child development and later outcomes (Ramírez‐Esparza et al., 2014). In China, research has significant disparities in identified disparities in child development cities between local urban households and their "peri-urban" counterparts, who are low SES, quasi-rural populations living within recently urbanized settings (Buckingham & Chan 2018). Yet little is known about the home language environment or parental investment among families living in peri-urban communities in China. This study uses a mixed-methods approach to examine the home language environment and early language development of young children age 18-24 months in peri-urban China and identify the impacts of economic constraints, time constraints and knowledge constraints on parental investment in a robust home language environment.

Methods We collected data on the home language environment and child language development from 81 households with children age 18-24 months in a peri-urban district in Chengdu, Sichuan. We collected and analysed two 16-hour audio recording from each household using the Language Environment Analysis (LENATM) system. We use two LENA-generated measures of the home language environment: Adult Word Count (AWC), the number of words spoken to or near the child by an adult; and conversational turn count (CTC), the number of adult-child alternations in conversation. Children's language development were assessed using the LENA-generated child vocalization count (CVC - a count of speech and speech-like productions made by the child) and the Mandarin version of MacArthur-Bates Communicative Development Inventory (CDI). We also selected 31 households from the quantitative sample to participate in semi-structured qualitative interviews about caregivers' childrearing experiences; knowledge, attitudes and beliefs about child development and parenting; the economic conditions of the household; the responsibilities and time demands on caregivers and other family members; and family dynamics within the household.

Results The mean for AWC and CTC scores among the sample were 12,354 (standard deviation=5,522) and 482 (standard deviation=262). The mean CVC score was 1,734 (standard deviation=749), and the mean for CDI is 37 (standard deviation=27). The results show large variation in both home language environment and child language development among the sample: the mean AWC and CTC for the top third of households in our sample (18,532 and 777, respectively) were both nearly three times higher than those of the bottom third (6,986 and 247, respectively), and the average CDI score for the top third of the sample (72.5) is six times greater than the mean score of the bottom third (12.5). Our qualitative interviews found that the primary factor limiting parents from effectively investing in a robust home language environment is a lack of accurate parenting knowledge among caregivers, due in large part to unreliable sources of information. Compounding knowledge constraints among caregivers,

time constraints (due to work outside the home and other household responsibilities) presented as a secondary barrier for many households interviewed.
Conclusion The results of this study indicate that large shares of children may be at risk for developmental delays due to inadequate investments in the home language environment. Policy makers and practitioners should promote knowledge of early childhood development and the importance of the home language environment to better support peri-urban caregivers of young children and maximize children's development.

Key words Language development, home language environment, parental investment, peri-urban communities
Reference Weisleder, A., & Fernald, A. (2013). Talking to children matters: Early language experience strengthens processing and builds vocabulary. Psychological science, 24(11), 2143-2152. Buckingham, W., & Chan, K. W. (2018). One city, two systems: Chengzhongcun in China's urban system. Journal of Contemporary China, 27(112), 584-595.

分类：3. Early Childhood Development 儿童早期发展
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Prenatal Environmental Antibiotics and Fetal Growth: A Biomonitoring-Based Prospective Study in Eastern China

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Background: As a class of emerging environmental contaminants, antibiotics may pose a potential threat to human health, especially in children. Thus far, it's not well understood whether prenatal environmental antibiotics exposure adverse fetal and postnatal growth.
Aims: Here we aimed to evaluate whether and to what extent environmental antibiotics exposure is associated with fetal l growth.
Methods: A total of 735 pregnant women and their full-term offspring from the Shanghai Obesity Birth Cohort were involved in the study. At enrollment, a face-to-face interview and a standardized food frequency questionnaire during pregnancy were used to gather maternal information. Maternal urine specimen was collected during the third trimester. Maternal urinary concentration of fifteen environmental antibiotics was measured by liquid chromatography-tandem mass spectrometry and enzymatic method. At birth, experienced obstetric nurse measured the newborns' anthropometric parameters. The associations between the maternal antibiotic levels and neonatal anthropometric parameters were examined by linear regression model, adjusting for potential confounders.
Results: Fluoroquinolones and sulfonamides, both used as s preferred-as-veterinary antibiotics or veterinary antibiotics (VA), were the most predominant antibiotics, with median creatinine-adjusted concentrations of 0.26 μg/g and 0.07 μg/g creatinine, respectively. Maternal VA concentration was negatively associated with birth weight and ponderal index [per natural-logarithm (ln)-unit: adjusted β (95% confidence interval, CI) = − 42.1 (− 74.0, − 10.3) for birth weight, −0.11 (− 0.19, − 0.02) for birth weight z-score, and − 0.03 (− 0.05, − 0.002) for ponderal index]. Regarding specific VA, each ln-unit increment of florfenicol concentrations was likely to be associate with 39.7 g (95%CI: − 69.3, − 10.1) reduced birth weight, and 0.02 g/cm3 (95%CI: − 0.04, − 0.00) reduced ponderal index. The association of ciprofloxacin (a PVA) and above neonatal anthropometric parameters showed a similar dose-response relationship to florfenicol.
Conclusion: Maternal exposure to low-dose VAs may adversely affect fetal growth. Florfenicol and ciprofloxacin, used as a VA or PVA, might be the main environmental antibiotics obstructing growth at birth.

关键字 Environmental antibiotic, Veterinary antibiotic, Anthropometric parameters, Birth cohort study, Maternal-fetal exposure assessment

Category: 3. Early Childhood Development 儿童早期发展
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Big data review on little people: A systematic review of early childhood development and parental training interventions in rural China

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Abstract Content Inadequate care during early childhood can lead to long-term deficits in skills (Grantham-McGregor et al., 2007). Parenting programs that encourage investment in young children are a promising tool for improving early development outcomes and long-term opportunities in low- and middle-income regions, such as rural regions of Central and Western China (Engle et al., 2011), where 70% of China's future labor force is growing up. The goal of this study is to conduct the first meta-analysis of all empirical studies focusing on early childhood development (ECD) in rural and migrant communities in China. We aim to achieve three specific objectives: first, to document the prevalence of developmental delays among young children (below the age of five); second, to identify the prevalence of stimulating parenting practices; and third, to assess the effectiveness of interventions that aim to increase engagement in stimulating parenting practices, increase parenting knowledge, and lower risks of developmental delay.

Methods We conduct a systematic review and meta-analysis to investigate the prevalence of early developmental delays and stimulating parenting practices as well as the effect of parental training programs on child development outcomes in rural China. We obtain data in English from EconPapers, PubMed, PsycARTICLES, Cochrane Library, Web of Science, and Scopus (Elsevier), and in Chinese from China National Knowledge Infrastructure (CNKI), Wanfang Data, and VIP Information. Search criteria include all empirical primary data studies published over the past 20 years (November 15, 2000–November 15, 2020). To identify studies that meet the established criteria, we screen records, extract data, and assess risk of bias in duplicate. We primarily extract data on the main outcomes of interest: children's risk of cognitive, language, and social-emotional delay; prevalence of stimulating parenting practices (i.e., reading, storytelling, and singing with children); and impacts of parenting programs on ECD outcomes, parenting knowledge, and parenting practices. We conduct frequentist meta-analyses of aggregate data and estimate random-effects meta-regressions. Certainty of evidence is rated according to the GRADE approach. This study is registered with PROSPERO (CRD42020218852).

Results We identify 19 observational studies on the prevalence of developmental delays and stimulating parenting practices for children under five years of age (n = 19,762) and ten studies on the impact of parental training programs on early child development (n = 13,766). Children's risk of cognitive, language, and social-emotional delays in the rural study sites (covering 14 provinces mostly in Central and Western China) is 45%, 46%, and 36%, respectively. Furthermore, we find that only 23%, 25%, and 45% of caregivers report that they read a book, told a story, or sang a song to the child over the past three days. Parental training programs that focus on child psychosocial stimulation (in rural study sites across 6 provinces in Central and Western China) have positive impacts on child cognition, language, and social-emotional development (0.26 SD [95% CI: 0.18–0.35 SD]; 0.17 SD [95% CI: 0.06–0.28

SD]; 0.14 SD [95% CI: 0.03－0.24 SD]). One of the underlying mechanisms of the success of parental training programs appears to be increasing caregiver engagement in stimulating parenting practices and increasing the parenting knowledge of caregivers (0.39 SD [95% CI: 0.24－0.54 SD] and 0.20 SD [95% CI: 0.11－0.28 SD], respectively).

Conclusion A first major finding is evidence that suggests that early developmental delays may be prevalent across rural communities of Central and Western China. The prevalence of cognitive delay of 45% is comparable to that observed in other developing regions (Grantham-McGregor et al., 2007). A second major finding is that parents in the rural study sites infrequently engage in stimulating parenting practices. The human development literature is unanimous in establishing that households with lower incomes in less developed regions on average invest less time and resources in their children (see, e.g., Engle et al., 2011). Third, our results support the effectiveness of parental training programs to improve ECD by encouraging parental engagement. With regard to optimal program design, we find that one-on-one parental training is effective for improving ECD; and that home-based interventions have a larger impact on child cognition than center-based interventions (0.34 SD versus 0.19 SD) due to lower compliance of more disadvantaged households to center-based programs. Future in-depth research on optimal program design is needed to shed light on how to provide more children, including the most disadvantaged ones, with a fair start in life.

Key words systematic review, early childhood development, parenting practices, parental training intervention, rural China,
Reference Engle, P. L., Fernald, L. C., Alderman, H., Behrman, J., O'Gara, C., Yousafzai, A., ... & Global Child Development Steering Group. (2011). Strategies for reducing inequalities and improving developmental outcomes for young children in low-income and middle-income countries. The Lancet, 378(9799), 1339-1353. Grantham-McGregor, S., Cheung, Y. B., Cueto, S., Glewwe, P., Richter, L., Strupp, B., & International Child Development Steering Group. (2007). Developmental potential in the first 5 years for children in developing countries. The Lancet, 369(9555), 60-70.

Category: 3. Early Childhood Development 儿童早期发展
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The home language environment in rural China: Evidence from rural and migrant populations

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Abstract Content The home language environment is a crucial input to a child's early language skills and lays the foundation for future development (Gilkerson et al., 2018). The home language environment may be particularly important in poor rural and migrant communities of China, where many children are developmentally delayed. Unfortunately, little is known about the home language environment in these populations. This study seeks to objectively describe the home language environment in rural and migrant Chinese populations and examine the household and family characteristics that influence this environment.

Methods We assessed the home language environment in 77 rural households and 81 migrant households. Two 16-hour audio recordings were collected and analyzed using the LENATM system (Ford et al., 2008). This system generates three key measures of the home language environment: Adult Word Count (AWC - number of adult words heard child), Conversational Turn Count (CTC - number of adult-child verbal alternations), and Child Vocalization Count (CVC - number of utterances by the child). We measured child language development using the MacArthur-Bates Communicative Development Inventories (CDI). This was administered alongside a demographic survey to all sample households. We conduct descriptive t-tests to compare the home language environment and child lagnauge development outcomes between rural and migrant households. We conduct univariate and multivariate correlational analyses to determine associations of household characteristics to measures of the home language environment, and we conduct additional multivariate correlational analysis to determine the role of demographic characteristics and home language environment measures on child development scores.

Results Among rural households, AWC, CTC, and CVC scores were of 15,783, 655 and 313, respectively. Among migrant households, AWC, CTC, and CVC scores were 12,354, 482 and 232, respectively. Rural households performed significantly better than migrant households: rural children had higher AWC by 3,429 ($p<0.001$), higher CTC by 173 ($p<0.001$), and higher CVC by 408 ($p<0.001$). Rural children also scored 17 points higher than migrant children in language skills measured by CDI (54 vs 37; $p<0.001$). Our correlational analysis found that maternal employment was positively associated with AWC and CTC (both $p<0.05$) among the full sample. In rural households, male gender was positively associated with AWC, CTC and CVC (all $p<0.05$) and being an only child was significantly associated with AWC and CTC (both $p<0.05$). For migrant children, only female gender was significantly linked to AWC ($p<0.05$), CTC ($p<0.01$) and CVC ($p<0.01$). All measures of the home language environment were positively and significantly correlated with child language development among the full sample and migrant subgroup, but AWC was not significantly associated with lagnauge development among rural children.

Conclusion The large gap between rural and migrant households revealed in this study is worrying, as the home language environment during early childhood can predict future cognitive outcomes. The home language environment scores in rural and migrant households are both below that of urban China. Policymakers should seek to improve

the home language environment in rural China, focusing especially on migrant households, as these children lag behind other populations by a large margin.

Key words Early childhood development, home langauge environment, language skills, rural China, migrant communities
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分类：3. Early Childhood Development 儿童早期发展
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The effect of COVID-19 Lockdown on Preschoolers' Total Daily Screen Time at Home in West China

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Since COVID-19 first appeared in Wuhan, China in December 2019, the epidemic has spread rapidly across the country. To reduce the spread of the infections, kindergartens have been closed for several months. Prolonged home confinement can affect children's behavior at home. Therefore, we investigated the effect of COVID-19 lockdown on preschoolers' total daily screen time at home in West China. In this cohort study, 1126 preschoolers were enrolled, whose parents completed an online survey from June 1st to 5th, 2020. The results showed that preschoolers' total daily screen time during lockdown was significantly longer than before lockdown (3.34±2.67h vs 1.87±1.72, p<0.001). The older age (OR 1.26, 95% CI 1.07-1.48), better annual household income (OR 1.13, 95% CI 1.01-1.27), and decrease of time spent outdoors (OR 1.52, 95% CI 0.37-0.72) and moderate-vigorous physical activity (OR 1.57, 95% CI 0.43-0.77) were independently associated with the increasing of total daily screen time. Preschoolers with longer screen-time were observed with higher proportion of bad temper (23.03% vs. 14.63%, p< 0.05), decreased attention (20.34% vs. 10.95%, p<0.001), and being scolding or corporal punishing (22.91% vs. 11.18, p<0.001). Our results suggest that preschoolers' total daily screen time obviously increased during lockdown. It might accompany with some psychological behavior problems and be adverse to the healthy development of children in early childhood. We should pay more attention to the physical and psychological health of children during the COVID-19 outbreak.

关键字 COVID-19 Lockdown; Preschoolers; Total Daily Screen Time; at Home

分类：3. Early Childhood Development 儿童早期发展
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Associations between infant metabolites at birth and growth trajectory in the first 2 years of life: a prospective cohort study

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Object: Previous studies suggested that blood metabolites at birth is closely related to birth weight, but its correlation with growth trajectory during the first several years after birth has seldom been reported. We tested the hypothesis that the index of plasma tandem mass spectrometry at birth may be correlated with the trajectory of children's BMI in the first two years after birth.
Methods: We recruited 848 mother-infant pairs from the Shanghai Birth Cohort, a prospective study, spanning 2013 to 2016. Fifty-eight kinds of metabolites status of blood in dried blood spot samples were measured. The BMI trajectories within the first two years of life were classified by latent class analysis. Stepwise regression was used to screen out risk factors related to the trajectory of persistently high BMI. ROC curves were plotted to evaluated the predictive performance of the models.
Results: Neonatal metabolites status of blood at birth were closely associated with growth trajectories during the first two years. In children with persistent high BMI trajectory, lower level of Gly(glycine) and higher levels of Tyr(tyrosine), C8:1 and C14 were determined. We identified a regression model adjusted for BMI, birthweight, and sex, found that Gly, Tyr, C8:1 and C14 can predicted persistent high BMI trajectory. ROC analysis of this model revealed AUCs of 0.846 (95%CI 0.806-0.880) for the detection.
Conclusions: Our findings suggested that amino acids and carnitine at birth may be important predictors for persistent overweight/obesity.

关键字 plasma tandem mass spectrometry , growth trajectory

分类：3. Early Childhood Development 儿童早期发展
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A comparison of the distance and the angle using the modified sit and reach test in preschoolers

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Objectives:This study compared the proposed angle and the commonly used reaching distance to verify the influence of the anthropometric characteristics in preschoolers.
Methods:194 preschoolers (119 boys and 75 girls) participated in the study. Before testing, the anthropometric characteristicswere collected. Each participant performed the modified sit-and-reach (MSR) test twice, using a sit-and-reach box. The distance score was obtained from the starting point to the reaching point, while the angle score was calculated according to the hip flexion angle. A Pearson's correlation was performed to study the association of the distance and angle scores with anthropometric characteristics. A paired t-test was performed to compare the difference between two normalized MSR results. Two-way ANOVA was used to investigate the effect of gender and age on hamstring flexibility in preschoolers using MSR scores.
Results:There was no significant correlation between the flexion angle and anthropometric measurements (r ranging from -0.006 to 0.041), while the reaching distance and anthropometric characteristics were found to be weakly correlated (r ranging from -0.149 to 0.339). There was no significant difference between two normalized MSR scores ($p>0.99$). A significant main effect of gender group was found in both MSR scores ($p<0.05$).
Conclusion:The calculation of the proposed flexion angle when performing the MSR test is feasible and appears to eliminate the concern regarding the limb length bias or the device limitation.

关键字 学龄前儿童，坐位体前屈，身体柔韧性

分类：3. Early Childhood Development 儿童早期发展
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Observation on the rehabilitation effect of a child with Absence of Fidgety movements with severe spasm of lower limbs

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Abstract: Objective To explore the methods of rehabilitation treatment for children with Absence of Fidgety movements (F-) accompanied by significantly increased muscle tone, so as to improve the rehabilitation effect and reduce the incidence of disability. **Methods** A case of Absence of Fidgety movements (F-) accompanied by significantly increased muscle tone was evaluated comprehensively, and an integrated Chinese and Western medicine comprehensive rehabilitation program was formulated. Including: classical exercise therapy, physical factor therapy, meridian conditioning, acupoint massage, wave training and use of bionic pastes , etc. A long course (Total 24 weeks) and an intensive treatment were given. The indexes of the children before and after treatment were compared and the therapeutic effect was evaluated. **Results** After treatment, the general motor, Fine motor, intelligence development, muscle tension and quality of exercise were improved obviously, and some indexes reached normal standard. **Conclusion** Professional rehabilitation treatment should be given as soon as possible to the children with Absence of Fidgety movements (F-) accompanied by significantly higher muscle tone, which can minimize the degree of disability, and finally achieve close to or normal development outcome, and improve the quality of the population.

关键字 cerebral palsy; infants; Absence of Fidgety movements ; Muscle tension; rehabilitation

Rare Diseases

罕见病

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Lipoprotein Glomerulopathy in China

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Background: Lipoprotein glomerulopathy is a rare kidney disease characterized by lipoprotein thrombi in the glomerulus. Here, we summarized the clinical features and genetic characteristics of lipoprotein glomerulopathy in China. Methods: We reviewed 18 pediatric and 156 adult cases of lipoprotein glomerulopathy reported in China from the year of creation to 2021. Results: In China, the number of pediatric LPG patients [12.0±2.90 years (range, 7－17years)] was less than adult patients [35.6±13.8 years (range, 18－72years)]. The most common clinical features were edema, hematuria, hypertriglyceridemia, and increased serum apoE levels. Extra-renal manifestations included anemia, splenomegaly, and cardiac lipoprotein deposition. There were 12 mutations have been reported, APOE Kyoto was the major LPG mutant in China, Homozygosity for E3 (E3/3) were in most cases (n=52, 29.9%). Conclusion: APOE Kyoto is the most common mutation in patients with lipoprotein glomerulopathy. In China, homozygosity for E3 (E3/3) is the most common isoform.

关键字 Lipoprotein glomerulopathy, China

分类：24. Rare Diseases 罕见病
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A novel splicing site mutation and a deletion of HPGD in a Chinese patient with mild primary hypertrophic osteoarthropathy: a case report and literature review

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Background: Primary hypertrophic osteoarthropathy (PHO) is a complex, genetically and clinically heterogeneous disorder. Clinical diagnosis is a challenge for pediatrician confronting with an incomplete clinical presentation. We aimed to analyze the clinical and genetic features of PHO patients with HPGD variation and provide useful information for early diagnosis.
Methods: Trio-based whole-exome sequencing was performed in a 22-month-old boy, with digital clubbing and fine coronary-to pulmonary fistula from birth. The biomarkers of bone metabolism were detected. Besides, previous literatures related to PHO with HPGD gene mutation were reviewed, up to March, 2021.
Results: A novel splicing site mutation c.421+1G>T and a deletion of exon 3 were identified in the HPGD gene, which accounted for the patient's clinical features. The bone turnover markers were increased beyond the normal range, except for the level of CTX-s coincided with the growth period. Through systematically reviewing previous studies, it found that the frequency of acro-osteolysis, hyperhidrosis, seborrnoea and delayed cranial suture closure were much lower in Chinese patients and almost all cases of PHO presented digital clubbing. Meanwhile, the c.310_311delCT mutation was likely to be a hotpot mutation site of Chinese origin; the c.175_176delCT mutation was reported as a hotpot mutation site for European population; and the c.418G>C mutation was thought as another mutational hotpot of Asian patients.
Conclusion: With the application of next-generation sequencing, the mutations in the HPGD gene were likely to be the important biomarkers for PHO diagnosis and treatment. Our report will enrich the clinical and variation spectra of PHO.

关键字 Primary hypertrophic osteoarthropathy, HPGD, hotpot mutation, Trio-based whole-exome sequencing, splicing site mutation, bone metabolism

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Analysis the characteristics of SLC25A13 gene variations of infantile intrahepatic cholestasis with unknown etiology

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Abstract Content To investigate the characteristics of SLC25A13 gene variations of infantile intrahepatic cholestasis with unknown etiology.

Methods Infants with intrahepatic cholestasis of unknown etiology who were hospitalized in the Department of Gastroenterology of the Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou Medical University from January 2016 to December 2020 were selected. Next generation sequencing was performed to select variations of SLC25A13 gene, and Sanger sequencing were using to identify variations of SLC25A13 gene. Additionally, the most frequent large fragment variations of SLC25A13 gene were also detected. Then, the characteristics and function of SLC25A13 gene variations were analyzed.

Results 30 infants with intrahepatic cholestasis were performed genetic testing. SLC25A13 gene pathogenic variants were detected in 12 cases. The frequency of SLC25A13 gene in infantile intrahepatic cholestasis was 40%. The most common variation was c.852_855delTATG, p.M285Pfs*2. A novel variation (c.1808T>C:p.L603P) was identified.

Conclusion Citrin deficiency caused by SLC25A13 gene variation might be the most important cause of infantile intrahepatic cholestasis with unknown etiology. Citrullinemia might take an significant role on the differential diagnosis. The novel variation, which impairs citrin function, has expanded the variation spectrum of SLC25A13 gene.

Key words Intrahepatie cholestasis; Infant; SLC25A13 gene; Variation

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Pedigrees analysis of children with short stature caused by novel ACAN gene mutation

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Background: *ACAN* (OMIM 155760) is located on chromosome 15q26 and encodes the production of aggrecan. Aggrecan is a large chondroitin sulfate proteoglycan with a molecular weight of 254 kDa and contains 2530 amino acids. It is a critical structural component of the extracellular matrix of cartilage, including growth plate, articular and intervertebral disc cartilage. It plays a key role in bone development.
Method: Here we describe three pedigrees with loss-of-function variants in *ACAN*. Whole exome sequencing was performed for the probands from each family. We illustrate the clinical variability associated with *ACAN* variants.
Results: The proband of pedigree 1 was a 4-year-10-month-old girl with short stature (88.6 cm, -5.06 SDS) and mild flat nasal bridge. Spine CT revealed incomplete lamina fusion in cervical 4 and head MRI suggested a pineal cyst. Next-generation sequencing (NGS) identified a novel heterozygous frameshift mutation c.1525delT (p.S509Rfs*31) in exon 8 of *ACAN* gene. Her parents and maternal grandparents were all short in stature (her father was 160 cm, her mother was 135 cm, her maternal grandfather was 165 cm, her maternal grandmother was 150 cm) and her mother had the same variant in the same site. The proband of pedigree 2 was a 7-year-9-month-old girl without obvious craniofacial deformities. She was a little short in height (120.1 cm, -1.06 SDS) and had bilateral breast development at about 7 years old. Both gonadotropin-releasing hormone (GnRH) stimulation test and uterine ovarian ultrasound supported central precocious puberty. X-ray imaging indicated that her bone age (BA) was advanced (10 years old). Lateral radiograph indicated abnormal vertebral development (the lumbar spine was slightly lateralized and the physiological curvature of the cervical spine became straight). NGS identified a novel heterozygous frameshift mutation c.2363delC (p.S790Qfs*20) in exon 12 of *ACAN* gene. Her parents and maternal grandfather were all short in stature (her father was 146.3 cm, her mother was 140 cm, her maternal grandfather was 150 cm) and her mother had the same variant in the same site. The proband of pedigree 3 was an 8-year-8-month-old boy, manifested as short stature (109.3 cm, -4.14 SDS), relative macrocephaly, mild flat nasal bridge, low-set ears, short neck and short thumbs. Growth hormone (GH) stimulation test suggested that GH was partially deficient. X-ray imaging indicated that BA was obviously delayed (5 years and 6 months). NGS identified a novel heterozygous frameshift mutation c.116dupT (p.R40Efs*51) in exon 3 of *ACAN* gene. His mother and maternal grandfather both had short stature (149 cm and 150 cm respectively), macrocephaly, short neck and the same variant in the same site. The mutation sites of *ACAN* gene in the three pedigrees were all discovered for the first time, and there was no related report in the past.
Conclusions: *ACAN* gene mutations can be clinically manifested as short stature, craniofacial deformities (including macrocephaly, low-set ears, etc.), abnormal vertebral development, and may also be associated with central precocious puberty. Most *ACAN* gene mutations are heterozygous mutations, and there was no significant correlation between the clinical phenotype and age, sex, mutation site, mutation type, etc. *ACAN* gene variants are important genetic factors for short stature and should be considered as the differential diagnosis of children with idiopathic short stature.

关键字 ACAN, short stature, craniofacial deformity, precocious puberty, whole exome sequencing

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Menkes disease diagnosed by a novel ATP7A frameshift mutation in a patient with infantile spasms—a case report

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Menkes disease (MD) is a rare congenital copper deficiency disease caused by an adenosine triphosphatase copper transporting alpha (ATP7A) gene mutation. It is a progressive and systemic disease that primarily involves the central nervous system and connective tissues. The clinical manifestation of these patients with MD is curly hair, progressive muscle tone reduction, and convulsions, and often leads to death in early infancy. Herein, we present a case of a 9-month-old Chinese male who displayed developmental regression, followed by convulsions, which were characterized by infantile spasms. The proband also had curly hair, hypopigmented skin, cutis laxa, decreased muscle tone, and micrognathia. The patient’s serum copper and ceruloplasmin levels were below the reference values. Brain magnetic resonance imaging showed abnormal signals bilaterally that were symmetrically distributed in the caudate nucleus, globus pallidus, and subcortical white matter of the temporal parietal cortex, white matter in the anterior and posterior corners of the ventricles and the anterior limb of the internal capsule. The electroencephalograph showed hypsarrhythmia. Genetic testing revealed a novel frameshift mutation in the ATP7A gene exon 13 and premature termination codon. Copper replacement therapy was initiated after the delayed diagnosis was established; However, the patient still died several months later due to disease progression. Our case reveals a novel frameshift mutation of the ATP7A gene, which expands the gene spectrum of MD. The infants with uncontrollable convulsions, regressive development, curly hair, MD should be considered at early stage and also need the further genetic analysis to confirm MD finally. The correct and timely diagnosis and initiating copper replacement therapy may improve the prognosis.

关键字 Adenosine triphosphatase copper transporting alpha; Infantile spasm; Menkes disease; Copper replacement therapy; Case report

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Delay diagnosis of achondroplasia — An appropriate prenatal diagnosis

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Achondroplasia is the most common disease in fetal nonfatal short limb bone deformity, which is mainly presents with limb shortening, short stature, and characteristic facial configuration. During fetal period, prenatal ultrasonography is the main means of disease screening. However, genetic examination is the diagnostic standard of achondroplasia, which can further guide pregnancy. We report a case of child whose limbs were short and proximal femoral shaft-epiphyseal angle was significantly abnormal during multiple ultrasound, but further Sanger sequencing method for FGFR3 gene c.1138 G > A detection was negative. Parents choose to continue pregnancy after doctor-patient communication. One year after birth, the patient developed asymmetrical short stature with motor retardation. Exon examination showed that FGFR3 gene c.1620 C > A was positive. As a new method for fetal medical diagnosis, fetal exon group sequencing will provide another new way for prenatal diagnosis of fetuses with ultrasonic abnormalities (one or more malformations) that cannot be identified by conventional examination techniques (such as karyotype and CMA), but it is necessary to understand the limitations of this technique in clinical application. When the negative results of genetic testing are inconsistent with clinical results, it is necessary to reanalyze the samples and give more appropriate pregnancy guidance. We expect to form a guide for further genetic examination of fetal limb shortness as soon as possible.

关键字 Achondroplasia，FGFR3 gene

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A de novo mutation of DVL1 with a new phenotype of congenital dislocation of hip----Robinow syndrome

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Background: Robinow syndrome is a rare genetic disorder, which affect the development of multiple systems. Due to low prevalence and considerable phenotypic variability, it has been challenging to definitively characterize features of Robinow syndrome. New features of Robinow syndrome appear frequently. Here, we present a clinical report of Robinow syndrome which was induced by a variant in DVL1.
Methods: We performed DNA extraction and whole-exome sequencing analysis to obtain genetic data on the patient. We subsequently analyzed the patient's clinical and genetic data.
Results: The patient's clinical manifestations were facial dysmorphisms, bilateral dislocation of hip joint and hearing impairment.
Conclusions: Our report reveals novel manifestation of Robinow syndrome-bilateral dislocation of hip joint. Our report expands the manifestations of Robinow syndrome and contribute to the refinement of the symptoms of Robinow syndrome. Moreover, we highlight the value of WES for diagnosing Robinow syndrome.
关键字 Robinow syndrome, WES, DVL1, bilateral dislocation of hip joint

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Primary erythromelalgia mainly manifested by hypertensive crisis: A case report and literature review

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Objective: Primary erythromelalgia (PEM) is a rare autosomal dominant single-gene disease commonly presenting during hypertensive crisis. Herein, we describe the main clinical features, diagnosis and treatment of a typical PEM case.
Methods: Medical records of an 8-year-old boy with PEM were analyzed retrospectively, which included clinical characteristics, follow-up information, and SCN9A (Sodium Voltage-Gated Channel Alpha Subunit 9) gene analysis.
Results: The 8-year-old boy had complained of abnormal paresthesia in his feet and ankles with burning sensation and pain for 2 years. The skin of both lower legs was red and underwent ichthyosis and lichenification. Genetic analysis confirmed the existence of a SCN9A gene mutation. The symptoms were gradually improved by treating with intravenous drip and oral administration of nitroglycerin to slow his heart rhythm.
Conclusion: PEM is characterized by skin ulceration, redness, elevated temperature, and severe burning pain primarily in both lower extremities. PEM can be diagnosed by genetic analysis. As this case demonstrates, treating with nitroglycerin as the drug of choice to control the hypertensive crisis significantly improved the symptoms of PEM and hypertension in this patient.

关键字 Keywords: Erythromelalgia; Pain; Nitroglycerin; Slow heart rhythm; Genetic diagnosis

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A novel RPGR frameshift variant in Chinese children causes complexed phenotype combining primary ciliary dyskinesia and X-linked retinitis pigmentosa

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Background: Mutation in the X-linked retinitis pigmentosa GTPase regulator (RPGR) gene mainly caused retinitis pigmentosa (RP), a sensory cilium related disorder. While RPGR mutants also would cause severe respiratory system illness, while limited data are available until now.
Methods: Here, we reported a patient with bronchiectasis, sinusitis, recurrent respiratory tract infection and chronic wet cough. Ciliary function test showed incoordinate ciliary beat pattern with reduced ciliary beat frequency. According to clinical and laboratory findings, we screened PCD related genes, and a novel frameshift mutation of RPGR was detected, which was well studied with RP. Then the fundus examination was conducted with our patient, and indeed showed RP phenotype. And we also overviewed the genotype and phenotype-oriented literature of RPGR-related PCD and compared to the findings of our patient.
Results: Mutations in RPGR mainly cause retinitis pigmentosa, rarely respiratory symptoms were reported, only a total of 7 patients with RPGR-related PCD were collected until now, including 6 reported patients of 2 non-consanguineous families from 2 published literatures up to July, 2021 and 1 patient reported by our study. These patients were from Polish (4), France (2) and China (1). Among these 7 patients with RPGR-related PCD, all of them were male, which consistent with the Mendelian Inheritance. Recurrent respiratory infection (100%) were major manifestations, most patients developed chronic cough (42.9%), bronchiectasis (42.9%) or sinusitis (28.6%); hypoxaemia (14.3%), hearing loss (14.3%), diffuse bronchiectasis distal obstruction (14.3%) were rare, but heterotaxy was never seen. 3 different RPGR variants were identified showing RP with respiratory syndrome. Among them, p.Gly52Arg and 631_IVS6+9del were reported previously, and our participant was identified a novel mutation from her mother.
Conclusion: RPGR variants are rare in PCD patients, and mainly cause retinitis pigmentosa. In clinical, the X-linked gene RPGR mutation also could be the cause of recurrent respiratory tract infection, which was usually ignored.

关键字 Primary ciliary dyskinesia; RPGR; retinitis pigmentosa; children

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Extralobar pulmonary sequestration in children with abdominal pain: a report of 4 cases and literature review

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Objective Pulmonary sequestration is a rare congenital pulmonary malformation, accounting for 0.15% ~ 6.40% of congenital pulmonary malformations. Pulmonary sequestration in children is often misdiagnosed and missed because of its special anatomical characteristics and lack of specific clinical manifestations. Four cases of extralobar pulmonary sequestration with abdominal pain as the main manifestation were analyzed, and the literature at home and abroad was reviewed to improve the understanding of the disease.
Methods The clinical data of 4 children with pulmonary sequestration diagnosed by enhanced CT and surgery in our hospital from July 2020 to October 2020 were analyzed retrospectively, and the literature at home and abroad was reviewed.
Results It is common in school-age children, often with abdominal pain or accompanied by chest pain and vomiting. Chest plain film or CT can show space occupying lesions and pleural effusion. There is no abnormal blood supply artery around the space occupying mass in some children. The affected side can be accompanied by pneumonia, atelectasis and pleural effusion, and the effusion increases rapidly in a short time, which is bloody pleural effusion. Sometimes the diagnosis was not clear before operation, so emergency thoracotomy was needed. Extralobar pulmonary sequestration complicated with pedicle torsion was confirmed during operation and pathology.
Conclusion Extralobar pulmonary sequestration lacks characteristic clinical manifestations. Once pedicle torsion and infarction occur, it is difficult to diagnose and easy to be misdiagnosed. When school-age children have abdominal pain or chest pain with vomiting, the possibility of extralobar pulmonary sequestration combined with pedicle torsion infarction should be considered. At present, the source of abnormal blood supply artery can be found by pulmonary CTA, which has become the first choice for the diagnosis of pulmonary sequestration.

关键字 children, insular lung, abdominal pain

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A novel mutation in FOXP3 gene leads to atypical manifestations of IPEX syndrome: a case report

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The immune dysregulation polyendocrinopathy enteropathy, X-linked syndrome (IPEX) is a rare genetic disease characterized by multiple immune disorders. The different mutations of FOXP3 gene may lead to different manifestations. Here we present a rare case of IPEX syndrome with a novel variant in FOXP3 gene. Clinical manifestations include autoimmune hemolysis, bronchiectasis, diarrhea, and proteinuria but not diabetes and other endocrine disorders. Whole-exon sequencing confirmed the diagnosis of IPEX syndrome. Supportive treatment did not ameliorate his symptoms and immunosuppressive therapy showed a promising efficacy. Our report would provide a reference for the diagnosis and treatment of IPEX syndrome.

关键字 rare disease

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The new compound heterozygous mutation of NUP Nephropathy: report of two cases and literature review

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Objective: Nucleoporin (NUP) nephropathy is identified as a rare monogenic cause of steroid-resistant nephrotic syndrome recently. Here, we provide the clinical and genetic data of two cases with NUP nephropathy and a literature review.

Methods：We reviewed the medical records and genetic testing results of 2 children with compound heterozygous mutation of NUP genes who presented as early-onset steroid resistant nephrotic syndrome and progressed into end-stage renal disease (ESRD) rapidly. We also studied the correlations between NUP gene mutations and clinical manifestations by reviewing the literatures published on PubMed Database (http://www.pubmed.com) up to January 2021. Seventy-four articles were retrieved initially and 21 articles were included finally after manual screen. We summarized the clinical manifestations by using standardized vocabulary provided in Human Phenotype Ontology (https://hpo.jax.org/).

Results: Two patients with newly diagnosed nucleoporin nephropathy who carried a compound heterozygous mutations in NUP107 and NUP93 gene respectively were reported. Both patients presented steroid-resistant nephrotic syndrome and progressed to end-stage renal disease in childhood. While the mutation c.1537+1G>A in NUP93 gene was previously described, the mutations c.460A>G and c.1085C>T in NUP107 gene and c.1472A>T in NUP93 gene were novel. We also summarized the phenotypic and genetic spectrum of nucleoporin nephropathy in 86 reported patients who carried 50 different mutations in 6 NUP genes (NUP107, NUP93, NUP205, NUP85, NUP133, NUP160). The majority of them were Asians (66/86, 76.7%). The most prevalent renal manifestation was nephrotic syndrome with focal segmental glomerulosclerosis (50/86, 58.1%). Although 80.8% (59/73) patients developed end-stage renal disease within the first two decades, their long-term prognosis after renal transplantation are favorable. Various extra-renal manifestations were found in 44.8% (26/58) of patients and neurological involvement was most common (22/26, 84.6%), including microcephaly (13/22, 59.1%), intellectual disability (12/22, 54.5%), and global developmental delay (10/22, 45.5%).

Conclusions: The renal manifestation of nucleoporin nephropathy is highly consistent that most patients suffered early-onset nephrotic syndrome with focal segmental glomerulosclerosis. More than half of the patients had extra-renal symptom concomitantly. Asians showed potential susceptibility to NUP nephropathy. Despite the limited reports, some genotype-phenotype correlations have been gradually revealed.

关键字 nucleoporin, hereditary nephropathy, end stage renal disease, children

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Treatment of mycophenolic acid and losartan in widespread Stiff Skin Syndrome: A case report

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Background: Although rehabilitation training remains a central part of managements in stiff skin syndrome (SSS), several medications has drawn increasing awareness in recent years owing to the potential efficacy. Objective: To increase awareness of potential therapeutic agents in SSS. Methods: Case report. Results: A 5-year-old female was referred to our hospital with complaints of skin induration and limited joint mobility. Skin induration was first noted on the left hip in her second year of life. Successively, similar manifestations developed at her left lateral thigh, bilateral thigh roots, groin area, abdomen and the area behind the left shoulder and upper arm, with movement limitation of left lower limb. She was the first child of non-consanguineous couple with unremarkable perinatal condition. Her cognitive development was appropriate, but her height was gradually behind the expected after the onset of disease. Physical examination revealed weight 17.4Kg (-1.0 SDS) and height 107cm (-1.9 SDS). Stiff skin in affected regions bounded tightly to the underlying tissues, accompanied with various degree of hypertrichosis. Mild pigmentation was noted in affected areas of abdomen and groin. Gait abnormality and limitation of left hip abductor capacity were noted, without joint swelling or pain during activity. Laboratory examination revealed normal routine blood tests, renal and liver function, myocardial enzymes, erythrocyte sedimentation rate, C-reactive protein and serum immunoglobin. Serum autoantibodies, rheumatoid factor, anti-cyclic peptide containing citrulline and antistreptolysin O were all negative. Normal serum C4 and basically normal C3 levels were observed. Serum levels of inflammatory factors (IL-2, IL-4, IL-6, IL-10, TNF, IFN-γ) were within normal range. Tests of urine routine, urine microalbumin, urine β2-microglobumin (β2-MG) and urine mucopolysaccharides all had normal values. Magnetic resonance imaging (MRI) of left thigh reveled slightly thickening of skin, with normal muscles, femur, medullary cavity, hip, and knee. A review of MRI in local hospital revealed pelvic obliquity with reduced size of the muscles of left glutes. Whole exome sequencing (WES) of peripheral blood excluded pathogenic or likely pathogenic variants of related genes (including Fibrillin 1 gene (FBN1), interleukin-17C gene (IL-17C), and other common genes in hereditary skin diseases). Histopathological examination of biopsied samples from left lateral thigh, stained by hematoxylin and eosin (HE) and Masson’s trichrome, revealed mild hyperkeratosis and hyperplasia of mucosal squamous epithelium, hyperplastic collagen fibers in the dermis, scarce perivascular lymphocyte infiltration in the superficial dermis, and well-preserved appendages. Adipocyte entrapment was noted. Alcian Blue stain revealed positive area in part of middle and lower dermis. Masson’s trichome staining revealed increased collagen fibers in dermis. Diagnosis of SSS was made. Regular rehabilitation training was taken as a basic and long-term treatment with guidance from rehabilitation therapist. According to literatures, mycophenolic acid (MPA) and losartan (LST) treatment were also recommended, which was accepted by her parents and initiated after written informed consent. LST was given at a dose of 12.5mg/d. Dose of MPA was managed by concentration test, which was first started at 0.18g Q12h but with a AUC measured higher as 62.2 ug•h/mL. After adjustments, MPA was finally selected as 0.18g/d and 0.36g/d alternating daily, maintaining an AUC between 26.1 and 44.4 ug•h/mL. Follow-

ups were regularly taken, while the size of induration area and the severity of stiffness were assessed monthly. After LST and MPA treatment for 8 months, her skin induration and joint limitation were stable, but without significant improvement. Conclusion: To our knowledge, this is the first case of combination therapy of MPA and LST in widespread SSS.

关键字 stiff skin syndrome; mycophenolic acid; losartan

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Antithyroid drugs induced antineutrophil cytoplasmic antibody associated vasculitis in children: report of three cases and literature review

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Objective: The clinicopathological features and prognosis of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) in children induced by antithyroid drugs were explored. Methods: The clinicopathological features, treatments and prognosis of three children with AAV induced by antithyroid drugs in the Department of Pediatric Nephrology and Rheumatology of our hospital were analyzed retrospectively, and the literatures were reviewed. Results: (1) Among the 3 cases, there were 2 girls and 1 boy, whose ages were 12.7, 13.8 and 13.1 years old, respectively. All patients had medication history of propylthiouracil (PTU) and/or methimazole (MMI) before onset. Initial manifestation was pallor and renal involvements with nephrotic proteinuria, hematuria and renal function abnormality were presented in all 3 cases, while 2 of them had hypertension. Extrarenal manifestations were also presented: case 1 presented with rash, arthralgia and cardiac insufficiency; case 2 had brain involvement with repeated convulsions; case 3 presented with arthralgia and lung involvement. They were all tested positive for P-ANCA and MPO-ANCA. Initial renal histopathology of the 3 cases were consistent with ANCA-associated glomerulonephritis, which were classified into sclerosis, crescentic and mixed class respectively. After eight months of treatments, repeated renal biopsy of case 3 had demonstrated progression to sclerosis class. Antithyroid drugs (PTU or MMI) were discontinued in three cases, and they were all treated with corticosteroid combined with intravenous pulse CTX therapy. Plasma exchange was performed in case 2 and case 3 due to rapidly progressive glomerulonephritis and disease recurrence(suspected pulmonary hemorrhage), respectively. Case 3 was treated with rituximab combined with mycophenolate mofetil after recurrence. The extrarenal symptoms relieved quickly after treatments in all cases. P-ANCA and MPO-ANCA became negative in case 1 and case 2 after 6 months of treatments but were persistently positive in case 3. Three cases were followed up for 24 months, 10 months and 12 months, respectively: case 1 was in CKD stage 2 with normal urinalysis; case 3 was in CKD stage 4 with nephrotic proteinuria and microscopic hematuria; case 2 was in CKD stage 5 and had sudden death at home at 10-month follow-up. (2) There were 27 pediatric cases with AAV induced by PTU and MMI reported. Symptoms of AAV appeared in children after an average administration of 37.5 months of PTU (the earliest was one month) and MMI (the earliest was 8 months). Kidney and lung were commonly involved, while brain was rarely involved. The pathological changes of kidney were crescent nephritis and necrotizing pauci-immune complex nephritis. The total remission rate was 93.3% after antithyroid drugs withdrawal and treatment with corticosteroids and immunosuppressive therapy, however, there were severe cases with progression to CKD stage 5, pulmonary hemorrhage and death. Conclusion: PTU and MMI can both induce AAV in children, which it may occur after short-term course of administration. Kidney and lung are commonly involved while brain involvement is rarely seen. Timely withdrawal of antithyroid drugs and proper treatments with corticosteroids and immunosuppressants can result in high remission rate, though there are still some severe cases. Nephrotic-range proteinuria, renal fibrinoid necrosis, immune-complex deposition and tubular atrophy may be the risk factors for poor prognosis.

关键字 Propylthiouracil; Methimazole; Antineutrophil cytoplasmic antibody; Vasculitis; Children

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MYH9 associated disorders with the onset of Henoch-Schönlein purpura nephritis: a case report

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Backgrounds：Henoch-Schönlein purpura (HSP) is one of the most common vasculitis in children. Nephritis is observed in about 30%~60% of children with HSP. The prognosis of HSP depends mainly on the severity of kidney involvement. MYH9-related disorders (MYH9-RD) are a spectrum of autosomal dominant (AD) disorders characterized by congenital thrombocytopenia, giant platelets, and leucocyte inclusions named Döhle bodies. Additional extra-hematological manifestations can also occur, which are mainly hearing impairment, cataract, and nephropathy. Both of these two diseases have varying degrees of kidney involvement, and their treatment is full of challenges and risks.

Methods: In this study, we summarized the clinical features and management of a child with MYH9-RD with the onset of Henoch-Schönlein purpura nephritis (HSPN) admitted in our department in 2016.

Results: Before admission, the course of the disease was two months. The first symptoms of this 7-year-old girl were rash on both legs, eyelid edema, and proteinuria, followed by muscle pain in both lower extremities and abdominal pain around the navel. In addition, the child showed binaural hearing loss, optic ganglion cell pathway injury. The child's father had hereditary thrombocytopenia, cataracts, visual impairment, kidney damage, and was treated with hemodialysis since the age of 18. Renal biopsy in another hospital was diagnosed as HSPN (Type V) with moderate or severe mesangial hypercellularity like this page. After admission, the urinalysis showed that urinary protein was 4+, red blood cell was 0-3/HP, and 24-hour protein excretion was 2.028g. In addition, the child’s platelets were very low, which did not meet the general performance of HSPN. However, her father had hereditary thrombocytopenia and kidney damage, so it was likely that the disease was inherited from her father. To further explore the causes of disease, the genetic test showed that the child was a heterozygous variant of the MYH9 gene, and the variation was inherited from her father. According to the clinical manifestations, renal biopsy results, laboratory characteristics and genetic test results, the child was diagnosed as Henoch- Schönlein purpura (HSPN, CKD stage 2); MYH9 associated disorders (binaural hearing loss; large optic disc cupping; thrombocytopenia). After admission, the child continued to be treated with low-dose corticosteroids combined with methylprednisolone, followed by mycophenolate mofetil and cyclophosphamide pulse therapy. Edema subsided, but proteinuria still existed. After the treatment with tacrolimus, the proteinuria of the child decreased. Subsequent treatment with cyclosporine and antihypertensive drugs, the child was in a stable induction therapy condition like this page. However, due to the refusal of the child’s parents, platelet transfusion was not given. The child's platelets were still at a low level.

Conclusions：In conclusion, the clinical manifestations of HSP are diverse, especially with the most severe kidney involvement. Renal biopsy and treatment should

be done as soon as possible. MYH9-related disorders caused by mutations of the MYH9 gene are rare but essential causes of chronic kidney disease. Moreover, the onset is usually hidden, and the diagnosis is difficult. Genetic test should be performed as soon as possible to confirm the diagnosis of MYH9-RD. In addition, the family history of the child is also an essential basis for diagnosis.

关键字 Henoch-Schonlein purpura (HSP),pediatric patient,MYH9-related disorders (MYH9-RD)

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Current performing status and practice of sweat conductivity test for cystic fibrosis in children

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[Purpose] This article analyzed the current operating status of sweat conductivity test for cystic fibrosis in several clinical laboratories around the world . Combined with the sweat conductivity guidelines and our cases, we summarized the operating procedures and precautions of sweat conductivity for the intend of improving accuracy.
[Method] Summarize some of the important details of the test and best practice recommendations to guide the operation by reviewing the guidelines on the operation of sweat conductivity issued by Cystic Fibrosis Funds, The Clinical Laboratory Standards Institute (CLSI), the UK Multidisciplinary Sweat Testing Working Group and published relevant research literature. The routine procedures for sweat conductivity test includes perspiration stimulation, perspiration collection, and perspiration analysis. Our department has independently carried out sweat conductivity test since 2014 year. We established a quality inspection team to manage daily operation specifications, instrument maintenance and analyzer calibration, etc.
[Result] A total of 580 cases were tested during the past 7 years, and 38 cases failed, with a total failure rate of 6.6%, which meets the international requirements for sweat conductivity testing. 38 cases of failure were analyzed as follows. The first is failure of sweat stimulation. 4 cases of stimulation failure caused by crying of children under 3 years old. 3 cases showed skin rashes, itching and other allergic manifestations when stimulated. The second is 20 cases sweat insufficient including 7 cases during water fasting and 6 cases of severe malnutrition and chronic dehydration. In addition, 3 cases were treated with penicillin during the collection period and 2 cases were fish scaly skin. And 2 cases were mild edema. The third problem was performing error. 4 cases failed for the reason that syringe reabsorbed sweat too fast which caused air bubbles in the coil. Another 2 failed cases were pushing sweat into conductance cell was too fast and the analyzer had no stable numerical value. In addition, 5 cases' results of sweat conductivity were inconsistent with the clinical manifestations of CF.
[Conclusion] The operation of sweat conductivity test involves a lot of details, and there is no unified guidelines and norms at present. The operation norms and management systems developed by our department based on existing literature can improve the operation detection rate and have certain guiding significance.

关键字 Cystic fibrosis; sweat conductivity; performing

分类：24. Rare Diseases 罕见病
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Intermediate stage of Citrin deficiency with nephrotic syndrome: a case report and literature review

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Backgrounds: Citrin deficiency is an autosomal recessive disorder caused by mutations in the SLC25A13 gene. It is characterized by 1) neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD); 2) intermediate/compensation stage with unique food preference from childhood to adulthood; and 3) adult-onset type II citrullinemia (CTLN2).Dietary therapy is the major therapeutic for the disease of intermediate stage. Eating too many carbohydrates and infection can trigger CTLN2. It is a rare disease, with an incidence of one in 17,000 in China, and associated with nephrotic syndrome is even rarer.Case: A boy was diagnosed with Citrin deficiency by genetic testing due to neonatal cholestasis and was given control diets for a long time. He had no symptoms with normal serum liver enzymes. He preferred eggs and meat not rice or fruit and other sweets. when he was one year old, he was diagnosed with hormone resistance primary with nephrotic syndrome. Urinary protein turns negative after hormone and Prograf treatment. At the age of 7 years and 3 months, he presented pneumonia and recurrence of nephrotic syndrome, mental fatigue, anorexia and vomiting of gastric contents and then he was transferred to our pediatric nephrology department for further treatment. Physical examination on admission revealed fatigue, mild systemic edema, audible fine moist rales, slightly distended abdomen, liver 2.5 cm below the right rib cage, spleen not palpable. On the next morning after admission, he had frequent vomiting and occasional irritability. On the 4th day after admission, he had confusion, gradually aggravated, systemic edema gradually aggravated, oliguria, poor digestion, abdominal distension, progressive enlargement of liver and spleen, progressive increase of blood ammonia, transaminase and bilirubin, with the highest values of ALT 5887 U/L, AST 21690 U/L, blood ammonia 212 umol/L, APTT 95.8 s, Fbg 1.97 g/L, the largest liver 11 cm below the right rib cage, hard texture, and the spleen 6 cm below the left rib cage. He was diagnosised with nephrotic syndrome, Adrenocortical dysfunction, acute liver failure, acute kidney injury and pneumonia. He received diet control therapy, medium-chain triglyceride powder (1-2g/kg·d) orally, partial intravenous nutrition and arginine to reduce blood ammonia, anti-infection, dehydration and diuresis, intravenous hormone, plasma exchange therapy for 3 times, bedside CRRT dehydration for 4 times, correct coagulation abnormalities and symptomatic and supportive therapy. His consciousness returned to normal on the 7th day of admission, liver enzymes returned to normal on the 11th day of admission, and urinary protein turned negative on the 18th day of admission.
Conclusions: The intermediate stage of Citrin deficiency combined with nephrotic syndrome makes its treatment more difficult. There were dilemmas and contradictions in the therapeutic.
Points of discusson: To prevent progression of the intermediate phenotype of Citrlin syndrome to CTLN2, dietary control is important, adequate protein intake and arginine supplementation should be provided, and complete protein restriction is not recommended even in the presence of hyperammonemia. Carbohydrate intake must be limited, and large amounts of carbohydrates and infections can impair the process of NADH reoxidation in patients with Citrin deficiency, resulting in acute onset or progression of the disease.

关键字 Citrin deficiency, nephrotic syndrome, adult-onset type II citrullinemia, neonatal intrahepatic cholestasis caused by citrin deficiency

分类：24. Rare Diseases 罕见病

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Assessment of serum ceruloplasmin for early diagnosis of Wilson disease in children

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Objectives:

Serum ceruloplasmin is one of the major diagnostic parameters for Wilson’s disease (WD). This study aims to define diagnostic criteria of serum ceruloplasmin for screening and early diagnosis of WD in children.

Methods:

Serum ceruloplasmin were measured in 317 WD patients, 21 heterozygotes, 372 healthy control children and 154 non-WD patients. Receiver operating characteristic (ROC) curve was used to determine the diagnostic accuracy of serum ceruloplasmin for WD in children.

Results:

Among healthy controls, serum ceruloplasmin was low before the age < 6 months, and then remain 29-34 mg/dL. 8.1% of healthy children had serum ceruloplasmin <20 mg/dL. Serum ceruloplasmin concentration in WD patients was significantly lower than that in non-WD children. Only 1.9% of WD patients had serum ceruloplasmin >20 mg/dL. Serum ceruloplasmin showed gender difference, higher in healthy boys than girls and also higher in asymptomatic WD boys than girls ($p<0.01$, $p<0.05$). Serum ceruloplasmin had genotype difference. WD patients with R778L homozygotes exhibited lower level of serum ceruloplasmin than WD patients without R778L ($p<0.05$). The ROC curve revealed that serum ceruloplasmin, at a cutoff value of 16.8 mg/dL, had the highest AUC value (0.990) with a sensitivity of 95.9% and a specificity of 93.6%.

Conclusions:

Serum ceruloplasmin is a reliable biochemical parameter for early diagnosis of WD in children older than 6 months. Gender and genotype difference of serum ceruloplasmin should be considered at diagnosis of WD. The cutoff value of serum ceruloplasmin <16.8 mg/dL may provide the highest accuracy for diagnosis of WD in children.

关键字 ceruloplasmin, Wilson’s disease ,early diagnosis

分类：24. Rare Diseases 罕见病
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The clinical and molecular characteristics of 104 children with hypophosphatemic rickets caused by PHEX gene mutation

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Objective: To characterize the clinical and genetic features of 104 children with hypophosphatemic rickets caused by PHEX gene mutations.
Methods: we retrospectively collected the clinical data of 114 children with X-linked hypophosphatemic rickets, and analyzed the genetic variants in the PHEX gene.
Results: 38 were males and 66 were females. The age of onset ranged from 6 months to 6.5 years. Ninety-six children were diagnosed with skeletal deformities, and 8 children were diagnosed through family examinations. Most of the children have obvious lower limb bending around 1 year after birth, abnormal walking gait, slow height growth. 64 cases of knee varus, 28 cases of knee valgus, 17 cases of pectus, and 10 cases of Rachitic rosary. The average blood phosphorus was 0.91 mmol/l (0.61-1.1), the average alkaline phosphatase was 641 U/L (223-1766). Genetic testing showed that 50 cases had spontaneous mutations in the PHEX gene, 12 cases were inherited from fathers, 33 cases were inherited from mothers, and 8 cases were not genetically tested for their parents. The types of gene mutations include missense mutations, insertion and deletion mutations, and large deletions.
Conclusions: This is the largest study of X-linked hypophosphatemic rickets in Chinese children. The study provided the clinical and molecular characterizations of the pediatric patients.

关键字 X-linked hypophosphatemic rickets， children

分类：24. Rare Diseases 罕见病
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Novel compound heterozygous TRPM6 gene mutations cause primary hypomagnesemia with secondary hypocalcemia

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Background: Primary hypomagnesemia with secondary hypocalcemia (HSH) is caused by loss-of-function mutations in TRPM6 gene encoding epithelial magnesium channel which is characterized by hypomagnesemia and secondary hypocalcemia associated with neurological symptoms. Here, we aimed to investigate the genetic defects of TRPM6 gene in a Chinese girl.Methods: The genomic DNA of the proband and the parents was extracted for whole-exome sequencing (WES). The candidate variants were validated by direct Sanger sequencing. Quantitative PCR (qPCR) was subsequently performed to confirm the TRPM6 gene deletion. The effect of variant on mRNA splicing was analyzed through a minigene splice assay in vitro.Results: The proband presented with generalized seizures, tetany and muscle spasms, which were refractory to anticonvulsant treatment. The trio whole-exome sequencing identified the proband carried compound heterozygous variants in the TRPM6 gene, a paternal derived deletion in exon 6 and a maternal derived splicing variant (c.1638+7A>G) in exon 14. The minigene splice assay confirmed that the intron c.1638+7A>G variant resulting in exon 14 skipping which caused the alteration of TRPM6 mRNA splicing. These variants were predicted to result in a complete loss of function of TRPM6. Conclusion: Our results support that the compound heterozygous variants in TRPM6 are responsible for HSH in the Chinese girl. A novel pathogenic splicing variant (c.1638+7A>G) in the intron 14 of the TRPM6 gene is found to disturb the normal mRNA splicing, suggesting that the non-classical splice variant play an important role in HSH, and identifying the variant will be essential for future effective genetic diagnosis.

关键字 Primary hypomagnesemia with secondary hypocalcemia, TRPM6, splicing variant

Category: 24. Rare Diseases 罕见病
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A mouse model of X-linked Alport syndrome caused by a de novo shift mutation in the collagen region of COL4A5 gene

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Abstract Content X-linked dominant Alport syndrome (XLAS) is a rare kidney disease in children caused by mutations in the COL4A5 gene. The clinical manifestations are progressive renal decline, and eventually only dialysis and kidney transplantation are required. Collagen region is the most important functional region of COL4A5 gene, but due to the large number of mutations in this gene and the lack of hot spot mutations, the pathogenicity determination of mutations has caused great difficulties. At present, there are only two mouse models with nonsense mutation of COL4A5 gene, but no mouse model with frameshift mutation in collagen region. In order to study the pathogenic mechanism of COL4A5 gene collagen region mutation, this study intends to construct a new COL4A5 gene collagen region mutation mouse model, and explore its pathogenic function.

Methods A child with renal failure was diagnosed with XLAS, and the mutation sites of the child and its parents were identified by whole exon sequencing. Using CRISPR/Cas9 technique, mutant mouse models were constructed and bred with this site as editing target. Urine protein and creatinine levels were measured weekly from 6 to 24 weeks of age in point mutation mice. Serum creatinine, urea nitrogen and albumin levels were measured at 8, 12, 20 and 24 weeks. Electron microscopy was performed on the kidneys of hemizygous and heterozygous mice at 8W and 25W, respectively.

Results A 16-year-old male child of XLAS presented with gross hematuria, proteinuria, bilateral sensorineural deafness, accompanied by progressive decline in renal function, and is undergoing hemodialysis. The parents and relatives of the boy had no relevant clinical manifestations. The whole exon sequencing indicated that there was a frame-shift mutation c.2440delG (P.gle814FS) in the collagen region of COL4A5 gene. Bioinformatics analysis showed that this mutation could lead to the truncation of COL4A5 protein, but no related reports of this mutation have been reported. The gene mutation was not detected by the parents' genetic test, suggesting that the mutation was a spontaneous new mutation of COL4A5 gene. Using CRISPR/Cas9 technique, COL4A5 gene mutant mice were successfully constructed and bred. Compared with wild-type mice, the urine protein/creatinine level of both XmutY and heterozygous XmutX mice increased significantly from 8 weeks of age, and the urine protein/creatinine level of XmutY mice was significantly higher than that of XmutX mice, which was consistent with the clinical manifestations of massive proteinuria in the children. Blood test results showed that XmutY mice showed significant increase in serum creatinine and urea nitrogen and significant decrease in albumin from the age of 8 weeks, and showed a rapid growth pattern, which was consistent with the progression of renal function in the mutant children. In XmutX mice, the renal function changes were relatively gentle, and no obvious renal function abnormalities were observed. Electron microscopy showed that XmutY mice showed uneven thickness of basement membrane at the age of 8 weeks, and XmutX mice

showed partial uneven thickness of basement membrane at the age of 25 weeks, suggesting that this mutation could lead to abnormal changes in the glomerular basement membrane.

Conclusion This study for the first time found a child with XLAS induced by Gly814fs, a new COL4A5 gene frameshift mutation in the collagen region, and successfully constructed a mouse model of COL4A5 gene frameshift mutation, whose phenotype was consistent with the clinical manifestations of the child, providing a valuable research basis for the follow-up precision treatment and mechanism discussion.

Key words Alport syndrome, COL4A5 gene, frameshift mutation, mouse model
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分类：24. Rare Diseases 罕见病
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Loss-of-Function Variants Within LMOD1 Actin-binding Site 2 Cause Pediatric Intestinal Pseudo-obstruction by Impairing Protein Stability and Actin Nucleation

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The *leiomodin1* (*LMOD1*) gene, encoding a potent actin nucleator, was recently reported as a potential pathogenic gene of megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS, OMIM 619362). However, only a single patient has been reported caused by *LMOD1* mutation and the underlying pathogenic mechanism remains unknown. Here we first described a male infant with *LMOD1* mutations presenting typical symptoms of pediatric intestinal pseudo-obstruction (PIPO) but without megacystis and microcolon. Two compound heterozygous missense variants (c.1106C>T, p.T369M; c.1262G>A, p.R421H) were identified, both affecting highly conserved amino acid residues within the actin-binding site 2 (ABS2) domain of LMOD1. Expression analysis showed that both variants resulted in significantly reduced protein amounts, especially for p.T369M, which was almost undetectable. The reduction was partially rescued by proteosome inhibitor MG-132, indicating damaged stability of mutant proteins, at least partially, through proteasome-mediated degradation. Molecular modeling and actin polymerization assay showed that variant p.R421H weakened intermolecular interaction between ABS2 and actin, thereby resulting in decreased activity of actin nucleation. This study reports an additional patient carrying biallelic loss-of-function variants in *LMOD1*, further supporting *LMOD1* as a pathogenic gene underlying visceral myopathy including PIPO and MMIHS, strengthens the critical role of ABS2 in LMOD1-mediated actin nucleation, and moreover, reveals an unrecognized role of ABS2 in protein stability.

关键字 Pediatric intestinal pseudo-obstruction, LMOD1, mutation

分类：24. Rare Diseases 罕见病
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Defining pathogenicity of NOTCH2 variants for diagnosis of Alagille syndrome type 2 by using a large cohort of patients

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Background: Alagille syndrome (ALGS) type 2 caused by mutations in NOTCH2 had genotypic and phenotypic heterogeneity, diagnosis in some atypical patients with isolated hepatic presentation could be missed.
Methods: By using 2087 pediatric patients with pediatric liver disease, NOTCH2 allele frequencies, in-silico prediction results, protein domains, and clinical features were analyzed to define pathogenicity of NOTCH2 variants for diagnosis of ALGS type 2.
Results: Among 2087 pediatric patients with liver diseases, significantly more NOTCH2 variants that were absent in gnomAD occurred in patients with hypertransaminasemia and γ-glutamyltransferase (GGT) elevation than in other variants (P=0.041). Significantly more NOTCH2 variants that were absent in gnomAD were located in protein functional domains when compared to other variants (P=0.038). When missense variants were absent in gnomAD and predicted to be pathogenic by at least three out of seven in-silico tools, they were significantly associated with hypertransaminasemia and GGT elevation (P=0.007). when the pathogenicity of NOTCH2 variants was defined, those patients with likely-pathogenic (LP) variants significantly presented as hypertransaminasemia with high GGT compared with those patients with likely-benign (LB) variants (P=0.0001). Significantly more patients with LP variants had extra-hepatic phenotypes of ALGS compared with those patients with LB variants (P=0.0015).
Conclusion:When NOTCH2 variants are absent in gnomAD, null variants and missense variants that were predicted to be pathogenic by at least three in-silico tools could be considered pathogenic in patients with high GGT hypertransaminasemia who previously missed the diagnosis of ALGS.

关键字 NOTCH2, Alagille syndrome, rare variants, the interpretation of sequencing variants

分类：24. Rare Diseases 罕见病
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Identification of genetic sequence variations associated with the pathogenesis of X-linked hyper-IgM syndrome

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Background: X-Linked Hyper-IgM Syndrome (X-HIGM) is a rare genetic primary immunodeficiency disease caused by mutations of the CD40 ligand gene (CD40LG). It is characterized by normal or elevated levels of IgM and markedly decreased serum IgG, IgA, and IgE levels. Patients with this syndrome are often prone to infections. Environmental and genetic (especially genetic mutation) factors may play an important role in etiology, development, and pathogenesis of X-HIGM.
Methods: DNA from a male child diagnosed as having X-HIGM and DNA from his healthy mother were used for whole-exome (next-generation) sequencing and targeted gene sequencing. The results were analyzed using Exome Aggregation Consortium data and the Genome Aggregation Database and were further validated using Sanger sequencing.
Results: Next-generation sequencing results indicated that the CD40LG gene in the child had a p.R203I variant. In addition, his mother was a carrier, suggesting that the child's p.R203I homozygous mutation was inherited from his mother. The functional prediction scores from SIFT, MetaSVM, and FATHMM software indicated that this genetic variant may be harmful.
Conclusions: Single variations in many exons of the CD40LG gene can lead to X-HIGM. Although the pathogenicity of the variant identified in the present study has not been previously reported, prediction software found that it would be harmful. Thus, CD40LG may be related to this genetic disease. Despite these limitations, our findings provided insight into X-HIGM pathogenesis and suggested a potential target for therapeutic drug development.

关键字 X-HIGM, whole-exome sequencing, targeted gene sequencing, sanger sequencing, CD40LG

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A Case of Baraitser-Winter Cerebro-Fronto-Facial Syndrome with a Novel Heterozygous Mutation in ACTB and Literature Review

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Background: Baraitser-Winter cerebro-fronto-facial (BWCFF) syndrome is caused by a heterozygous gain-of-function mutation of ACTB and ACTG1 that encodes actin. The clinical features include intellectual disability, trigonocephaly or metopic ridging, arched eyebrows, hypertelorism and ptosis. Pachygyria or lissencephaly and colobomata are the main diagnostic basis of BWCFF.
Case Description: Here, we report an eight-year-old girl who had distinct facial features, including hypertelorism, arched eyebrows, wide nasal tip, low-set ears and thin upper lip. In addition, she also showed short stature, funnel chest, stunted growth, refractory epilepsy and brain abnormalities. Targeted gene panel sequencing identified a novel heterozygous missense mutation (c.587G>A) (p.Arg196His) in ACTB.
Conclusion: BWCFF should be highly suspected in patients with typical facial features and cortical malformations. High-throughput gene sequencing is an important means of diagnosis. However, further research is needed to understand the mechanisms behind phenotypes caused by functional loss mutations.

关键字 Mutation; ACTB; ACTG1; Baraitser-Winter cerebro-fronto-facial syndrome;

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Newly detected rare genomic variations in MMACHC are associated with methylmalonic aciduria: A case report and literature review

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Objective: To identify novel genetic variants in the metabolism of the cobalamin associated C (MMACHC) gene encoding the cblC protein that may be associated with the pathogenesis of methylmalonic aciduria (MMA).
Methods: DNA from a 7-month-old female infant diagnosed as having MMA, together with DNA from her healthy father and mother, was used for whole-exome (next-generation) sequencing and targeted gene sequencing. The results were analyzed using Exome Aggregation Consortium data and the Genome Aggregation Database, and the findings were confirmed using Sanger sequencing.
Results: Next-generation sequencing results indicated that the MMACHC gene in the infant had previously unreported compound heterozygous variations. Her father and mother were carriers, suggesting that the infant's heterozygous variant was inherited from them.
Conclusions: Numerous variations in different exons of the MMACHC gene are capable of contributing to MMA. The pathogenicity of the variants identified in the present study have not been previously reported; however, prediction software found that they would likely be harmful. The predisposition to MMA appears to be inherited. Our findings inform understanding of MMA pathogenesis and suggest a basis for providing pharmacological therapy for the presented patient.

关键字 MMA; MMACHC gene; whole-exome sequencing; targeted gene sequencing; Sanger sequencing; cblC type

分类：24. Rare Diseases 罕见病
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Progressive Cholestasis: Severe Phenotype of MEGDEL Syndrome with SATB2-associated Syndrome

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Background: MEGDEL syndrome and SATB2-associated syndrome (SAS) are both rare congenital disorders with poor prognoses caused by gene mutations. Method: We present the case of a 2-day-old girl with an unexplained abnormal liver function, feeding problem, and dystonia. Using next-generation sequencing to look for the etiology. Result: We identified two novel mutations in SERAC1 and a mutation in SATB2. Now, she is 15 months old and has the characteristics of SAS, such as downslanting palpebral fissures and delayed primary dentition. Besides the typical phenotypes of MEGDEL syndrome, such as hypertonia, failure to thrive, deafness, and motor regression, she has progressive cholestasis and is prone to high serum lactate after rehabilitation training and hypoglycemia with low ketone under starving conditions. Conclusion: The phenotype of progressive cholestasis substantially differ from the transient liver function abnormalities and hypoglycemia reported in the literature.

关键字 MEGDEL syndrome, SATB2-associated syndrome, phenotype, next-generation sequencing, follow-up

分类：24. Rare Diseases 罕见病
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A case of infantile-onset cystic fibrosis misdiagnosed as cardiomyopathy and analysis of new compound heterozygous mutation

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Objective: To report the clinical features and gene mutation characteristics of cystic fibrosis (CF) in an infant who was misdiagnosed as cardiomyopathy in the hospital, so as to improve clinicians' better understanding of CF disease and reduce misdiagnosis and missed diagnosis.
Methods: A retrospective analysis was used to summarize the clinical data of a child with CF admitted to the Pediatric Hospital of Fudan University in April 2021, according to which to share the diagnosis and treatment process and conduct genetic testing and analysis.
Results: A one year and ten months old boy was admitted to our hospital because of ″repeated edema and shortness of breath for more than 5 months, with aggravated symptoms for 20 days″. The local hospital considered the diagnosis as right ventricular cardiomyopathy. The child presented with poor appetite of solid food and growth failure since 10 months of age. Recurrent exacerbations of cough and sputum were noted from 1 year old, with malodorous steatorrhea sometimes. Physical examination indicated a thin and malnutritional stature, tachypnea and wheezing. Laboratory test revealed hypoproteinemia, decreased fat-soluble vitamins and fecal elastase of less than 0.5ug/g (reference value>200). The concentration of sweat chloride was as high as 125 mmol/L. The indexes of liver cirrhosis were elevated, in combination with mildly increased alanine aminotransferase and serum creatine kinase. Sputum culture was negative. CT showed pneumonia, nasal sinusitis, abnormal lung tidal respiratory function, and severe obstructive ventilatory dysfunction. B-ultrasound of liver showed hepatomegaly. A small-size pancreas infiltrated with fat was demonstrated in MR. Genetic testing revealed two compound heterozygous mutations in CFTR, i.e. c.1209+1G>C splicing mutation (maternal origin) and c.2475_2478dupCGAA frameshift mutation (paternal origin), both of which are predicated as pathogenic variants. The former is primarily reported to be pathogenic in patients with congenital absence of the vas deferens in China, and the latter is a novel frameshift mutation.
After administration of antibiotics, nebulization, albumin infusion, supplementation of fat-soluble vitamins and pancreatin, the child's cough alleviated, no further edema and tachypnea recurred, and his weight gain was satisfactory.
Conclusion: CF is a hereditary disease in an autosomal recessive pattern. The incidence of CF in China may be underestimated. In clinical settings, children with recurrent pulmonary infections，malnutrition and pancreatic insufficiency should be considered as possible CF. Early detection of sweat chloride and pancreatic function may be helpful for confirmation. Genetic testing is recommended to uncover the pathogenic mutations, thus to improve the recognition of CF.

关键字 cystic fibrosis; gene

分类：24. Rare Diseases 罕见病
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Twelve new cases of Schaaf-Yang syndrome in critically ill infants from the China Neonatal Genomes Project

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Objective: Schaaf-Yang syndrome (SYS) is a recently identified rare neurodevelopmental disorder characterized by neonatal hypotonia, feeding difficulty, joint contractures, autism spectrum disorder and development delay/intellectual disability (DD/ID). It’s mainly caused by truncating variants in maternally imprinted gene MAGEL2 which is within Prader-Willi Syndrome critical region 15q11-q13. To date, more than 120 SYS patients have been reported worldwide. Clinical diagnosis of SYS is difficult for a physician due to its rarity and highly variable phenotypes. This study aims to raise the awareness of SYS in critically ill infants and to promote accurate early diagnosis and comprehensive treatments with better benefits.

Methods: We retrospectively investigated the mutation spectrum and phenotypic features in a cohort of critically ill infants from the China neonatal genomes project (CNGP). Genetic tests were performed by clinical exome sequencing (CES)/exome sequencing (ES), and the clinical medical records were reviewed retrospectively. We also performed a review of relevant literatures.

Results: Twelve unrelated Chinese infants were diagnosed with SYS based on genetic testing. All of them carried truncating variants on paternal MAGEL2 allele with six previously unreported mutations: p. Met1195Cysfs*4, p. Gln339*, p. Thr217Hisfs*22, p. Ser950Alafs*6, p. Gly883Alafs*21 and p. Trp368*. Our patients presented with early-onset DD/ID, feeding difficult, hypotonia, infectious, respiratory distress and multiple congenital defects. Notably, we found that 11 of our patients presented with congenital heart diseases especially atrial septal defect. Furthermore, in molecular level, we demonstrated that the hot spot variants and fetal mutations cluster in the end of N-terminal region.

Conclusion: Our findings expand the genotype spectrum of SYS and indicate that congenital heart disease may be a common phenotype of critically ill infants with SYS in China. This study could provide a new insight into SYS.

关键字 MAGEL2, Schaaf-Yang syndrome, critically ill infant, truncated variant, atrial septal defect;

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Renal damage in inherited tyrosinemia type 1 (HT1) caused by novel compound heterozygous mutations of FAH: a case report

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Abstract
Background
Hepatorenal tyrosinaemia or hereditary tyrosinemia type 1 (HT1) is a rare inherited metabolic disease characterized by severe liver and renal disfunction. We noticed a case that the clinical manifestations mainly exhibited hepatosplenomegaly accompanied by the significant increase of the blood tyrosine and succinyl acetone in blood and urine, as well as renal damage with hematuria and proteinuria, which accorded with the gold standard of clinical diagnosis of HT1. With whole exome sequencing (WES) and Sanger sequencing, we have identified the novel compound heterozygous mutations (c.657delC(p.K220Rfs*12), c.607G＞A(p.A203T)) in the fumarylacetoacetate hydrolase gene (FAH), encoding the last enzyme of the tyrosine breakdown cascade. To verify the pathogenicity of the mutations, the clinical phenotype of the proband was summarized and the pathogenicity mechanism was further explored.
Method
(1) The clinical data of blood and urine tandem mass spectrometry and organic acid detection in probands were analyzed. (2) Bioinformatics analysis of the variants: conservative analysis of amino acid in mutation sites, prediction analysis of protein domain and three-dimensional structure. (3) Observation of pathological changes of renal biopsy tissues: HE, Masson, PAS, PASM staining and electron microscope observation of pathological changes of glomerulus and renal tubules. (4) Immunohistochemistry (IHC) was used to detect the expression of FAH, immunofluorescence (IF) was used to detect the localization and expression differences of Synaptopodin, the glomerular podocyte marker, and Cubilin and Megalin, the important receptors that are responsible for protein reabsorption in the proximal tubule. 5) The recombinant plasmids of wild type and mutant protein expression of FAH were constructed, and the expression of variants protein was verified in vitro. The ability of variants to regulate FAA metabolism was detected under FAA stimulation.
Results
(1) The A203T localized to an evolutionarily highly conserved region in FAH and both mutations are predicted to change the three-dimensional structure of proteins. (2) Electron microscope showed segmental fusion of glomerular foot processes, and biopsy showed structural damage of glomeruli and renal tubules. (3) IHC found that the expression of FAH in renal biopsy tissues of the proband showed a cliff-like decline. IF showed that the expression and localization of COL4A3 and COL4A5 in the basement membrane were normal, the linear structure of Synaptopodin was damaged, and the expression and localization of Cubilin and Megalin were abnormal. (4) In vitro experiments suggested that c.657delC(p.K220Rfs*12) in FAH affects the FAH expression and c.607G＞A(p.A203T) affects its function.
Conclusion
We report for the first time that the novel compound heterozygous mutations of FAH in a recessive manner are responsible for HT1. The novel mutations resulted in abnormal expression and function of FAH protein accounting for accumulation of FAA, which lead to severe liver failure accompanied by renal glomerular filtration barrier

dysfunction and abnormal protein reabsorption of renal tubules. We approached this issue to provide an important reference for further genetic counselling and testing for HT1 mutations in FAH.

关键字 Inherited tyrosinemia type 1 (HT1),FAH,Renal damage,Novel compound heterozygous mutations

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Identification of Novel Mutations in CUBN Associated with Chronic Isolated Proteinuria

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Proteinuria, a primary marker of kidney damage, is associated with poor outcomes in CKD patients. However, whether all forms of proteinuria are damaging still leaves some issues to be studied. Recently, genetic factors in the development and progression of chronic kidney diseases (CKD) have been cuased for concern. Nevertheless, the mechanisms underlying this process remain unclear. Cubilin, encoded by CUBN, is a multiligand endocytic receptor with a critical role in renal protein reabsorption, dysfunction of which exhibits isolated-proteinuria. But so far few researches available have addressed the CUBN polymorphism on proteinuria. Our study found the novel compound heterozygous mutations (c.4397G>A(p.C1466Y), c.6796C>T(p.R2266X), c.5153_5154delCT(p.S1718X) and c.6821+3A>G). To demonstrate pathogenicity of the mutations in CUBN, clinical and pathological data were analyzed retrospectively, and the mechanisms were investigated in vitro experiments.
Methods: (1) The probands with isolated proteinuria were offered clinical evaluation and genetic testing. Sanger sequencing demonstrated that the existence of the compound heterozygous mutations inherited separately from parents.(2) Bioinformatics analysis was performed using evolutionary tree, conservation of the mutation sites among different species, domain analysis, and three-dimensional structure prediction.(3) The tissues were stained with different staining techniques including hematoxylin and eosin (HE), periodic acid-Schiff (PAS), periodic acid-silver methenamine (PASM), and electron microscopy. (4) Cubilin was subjected to immunohistochemistry (IHC) and immunofluorescence (IF) was performed to detect the expression and location of Megalin/AMN.(5) Immunofluorescence was applied to examine the expression and possible co-localization of specific proteins (Cubilin and AMN) in vitro.
Results:(1) Both probands did not exhibit immune dysfunction, except elevated urinary albumin concentration, α-1-microglobulin and transferrin. (2) Meanwhile, the mutations had no effects on glomerular filtration barrier as evidenced by normal kidney morphology, no abnormalities appeared in foot process or basement membrane, and normal expression and localization of synaptopodin, WT1, type IV collagen. (3) Significantly, the expression of Cubilin dropped sharply accompanied by abnormal expression and location of AMN instead of Megalin, which froms the uptake receptor complex that is critical to receptor-mediated tubular reabsorption. (4) Furthermore, Our research found that partial suppression of Cubilin in renal biopsies from DKD, FSGS and MCD, could be compensated by the expression of AMN to maintain the reabsorption function of renal tubules. (5) Remarkably, the contact was disturbed in the probands.
Conclusion: We have identified the novel compound heterozygous mutations (c.4397G>A(p.C1466Y), c.6796C>T(p.R2266X), c.5153_5154delCT(p.S1718X) and c.6821+3A>G) in CUBN exhibiting chronic isolated proteinuria without progressive glomerular filtration barrier damage. The findings will assist in understanding the pathogenesis and mechanism of isolated proteinuria from a genetic

perspective. Also, it will provide reference for clinical application and prenatal diagnosis.

关键字 CUBN; Chronic Isolated Proteinuria;

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Adipose tissue development and adipogenesis are dysregulated in Prader-Willi syndrome

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Background: Prader-Willi syndrome (PWS) is a complex multisystem imprinting disorder caused by the expression loss of paternally inherited genes on the chromosome 15q11-q13. Childhood-onset morbid obesity and endocrine dysfunction are clinically hallmark features of PWS, although the underlying mechanisms remain elusive. Here, we first show that the adipose tissue development is disrupted in PWS infant patients and the white- and beige-adipogenesis processes are impeded in PWS mesenchymal stem cells. Additionally, we further intend to explore the detailed molecular mechanisms involved.
Method: We collected inguinal subcutaneous fat tissues from PWS infants and healthy control subjects and carried out histological and morphometric analysis. Isolated adipose-derived mesenchymal stem cells (ADMSCs) were cultured and induced to white and browning adipogenesis in vitro, respectively, via standard adipogenic mediums. The adipogenesis degree of differentiated adipocytes were analyzed according to lipid droplet accumulation, triglyceride content measurements, and adipocyte marker gene expression. Besides, in the mature beige adipocytes, thermogenic capacity assessed by β-agonist and cooling stimulation, mitochondrial content and the mitochondrial stress assay were examined through corresponding assays. Additionally, purified ADMSCs were applied to high-throughput RNA sequencing and bioinformatic analysis.
Results: The adipose tissue of PWS infants exhibited marked adipocyte hypertrophy and a decrease in UCP1 expression. During the course of adipogenesis, the gene program of white- and beige-adipogenesis was directly impaired in PWS ADMSCs along with dysregulated functions of mature adipocytes that the expression of adipogenic marker genes decreased, lipid accumulation and triglyceride content reduced, and leptin and adiponectin release levels were abnormal. Differentiated PWS beige adipocytes also showed impaired thermogenic ability with interfered thermogenic gene expression, decreased mitochondrial content, and disrupted mitochondrial respiration and oxygen consumption. Besides, we identified aberrant transcriptomic signatures in PWS individuals compared with controls characterized by differentially expressed genes relevant for insulin resistance signaling and angiogenesis pathway and significantly extensive alterations in precursor mRNA alternative splicing including adipogenesis regulators.
Conclusions: We conclude that PWS infants have abnormal adipose tissue development before childhood obesity occurred. The processes of white and beige adipogenesis and related adipocyte functions were impaired in PWS ADMSCs, leading to endocrine and metabolism disorders in PWS. Furthermore, these novel findings into adipose tissue development provide putative new strategies of diagnosis and treatment potentials to PWS and other obesity-related disorders.

关键字 Prader-Willi syndrome; obesity; adipose tissue development; adipogenesis

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Presence of Lipid Vacuoles in Kupffer Cells as a Marker for Early Detection of Niemann-Pick Disease Type C in Neonatal Cholestasis

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Aims: To explore the significance of lipid vacuoles in Kupffer cells for early detection of Niemann-Pick disease type C (NP-C) in neonatal cholestasis (NC).
Methods: This study enrolled NC patients with unexplained causes who underwent liver biopsy between January 2018 and December 2020. NP-C was diagnosed by genetic testing. To expand the sample size, this study also enrolled NP-C patients diagnosed between January 2015 and December 2017. Clinical data were retrieved from their medical records.
Results: A total of 168 NC patients with unexplained causes were enrolled, and 26 detected lipid vacuoles in Kupffer cells from liver biopsy. NP-C was diagnosed in 6 out of the 26 patients (23.1%), comparing to none of the 142 NC patients without vacuolar Kupffer cells (P <0.001). A total of 9 NP-C patients were identified as 3 additional NP-C patients were diagnosed between January 2015 and December 2017, and 16 distinct NPC1 variants were identified. Seven underwent liver biopsy at ages ranging from 35 to 112 days. Lipid vacuoles were detected in Kupffer cells by CD68 staining in all 7 liver tissues: the amount increased with age and the size became enlarged in the early disease course. Foam cells were observed in only 2 patients having obvious enlarged Kupffer cells with lipid vacuoles. Of the 9 NP-C patients, 7 presented as neonatal cholestasis with low GGT and 4 had fasting hypoglycemia.
Conclusions: Lipid vacuoles in Kupffer cells from liver biopsy can serve as a screening marker for early detection of NP-C in NC.

关键字 neonatal cholestasis; Niemann-Pick disease type C; Kupffer cell

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Treatment of scalp with 2% supramolecular salicylic acid in epidermolytic hyperkeratosis ichthyosis caused by KRT10: a case report

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Background

Epidermolytic hyperkeratosis caused by mutations in the genes that encode either Keratin 1 or Keratin 10 is a rare autosomal dominant skin. Most those patients present with scalp desquamation, sometimes with adherent thick scales requiring treatment. Shampoos are cosmetically acceptable but may be less effective. The application of a layer of emollient or keratolytic may be necessary but time-consuming. Safe, effective and convenient treatment is scarce in children.

Objective

This study aims to explore safe, effective and convenient treatment of removing adherent scales of scalp in children with epidermolytic hyperkeratosis.

Methods

A 4-year-old boy, who was diagnosed as epidermolytic hyperkeratosis with a de novo KRT10 c.466C>T mutation, was followed up since birth. He present with severe hyperkeratosis throughout the whole body, but absence of severe palmoplantar hyperkeratosis. He carried bothersome adherent thick scales. All the shampoos didn't work. We prescribed 2% supramolecular salicylic acid shampoo to treat the scalp. Apply the shampoo for 10 minutes per day when showering and then wash out. Photos were taken at 2,4 and 6 weeks respectively.

Results

The adherent thick scales of scalp were improved markedly. No adverse reactions occurred. The use of 2% supramolecular salicylic acid shampoo is very convenient.ConclusionsOur study provide potential blueprint that 2% supramolecular salicylic acid shampoo may be a kind of safe, effective and convenient skincare of removing adherent scales in children with epidermolytic hyperkeratosis.

关键字 supramolecular salicylic acid; Epidermolytic hyperkeratosis; KRT10; Scalp

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Neonatal cholestasis is an early liver manifestation of children with acid sphingomyelinase deficiency

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Objectives: To describe and summarize the liver manifestations of children with acid sphingomyelinase deficiency (ASMD) in the early disease course.
Methods: This study enrolled inpatients confirmed to have ASMD between July 2016 and December 2020. ASMD was diagnosed by genetic tests and / or an enzyme assay for ASM activity. Clinical data was gathered from their medical records.
Results: Eight pediatric inpatients were diagnosed as ASMD with 12 known disease-causing pathogenic variants identified. Hepatosplenomegaly, elevated transaminases, and liver foam cells were observed in all 8 ASMD patients when they were referred for liver subspecialty evaluation at age ranging from 4 months to 32 months. Of them, cherry red spot was only detected in 4 patients, development delay in 3 patients, and interstitial lung diseases in 1 patient. Three ASMD patients developed jaundice around 1 month of age, and cholestasis with high γ-glutamyl transpeptidase (GGT > 100U/L) was confirmed by liver function tests. Jaundice resolved at age ranging from 3 months to 10 months, but elevated transaminases and hepatosplenomegaly persisted. The 3 ASMD patients presenting as neonatal cholestasis died within 4 years of age. Apart from a CFTR heterozygous pathogenic variants, c.3209G>A (p.R1070Q), no additional pathogenic variant was identified in other cholestasis causing genes.
Conclusions: As ASMD can lead to neonatal cholestasis in the early disease course, it should be considered as a differential diagnosis of neonatal cholestasis.

关键字 acid sphingomyelinase deficiency; neonatal cholestasis; foam cell

分类：24. Rare Diseases 罕见病
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Genetic spectrum and clinical characteristics of 3β-hydroxy-Δ5-C27-steroid oxidoreductase (HSD3B7) deficiency in China

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Background
Biallelic variants in HSD3B7 cause 3β-hydroxy-Δ5-C27-steroid oxidoreductase (HSD3B7) deficiency, a life-threatening but treatable liver disease. The goal of this study was to obtain detailed information on the correlation between the genotype and phenotype of HSD3B7 deficiency and to report on responses to primary bile acid therapy.
Methods
The medical records of a cohort of 39 unrelated patients with genetically and biochemically confirmed HSD3B7 deficiency were examined to determine whether there exist genotype-phenotype relationships in this bile acid synthesis disorder.
Results
In all, 34 of the 44 variants identified in HSD3B7 were novel. A total of 32 patients presented early with neonatal cholestasis, and 7 presented after 1-year of age with liver failure (n=1), liver cirrhosis (n=3), cholestasis (n=1), renal cysts and abnormal liver biochemistries (n=1), and coagulopathy from vitamin K1 deficiency and abnormal liver biochemistries (n=1). Renal lesions, including renal cysts, renal stones, calcium deposition and renal enlargement were observed in 10 of 35 patients. Thirty-three patients were treated with oral chenodeoxycholic acid (CDCA) resulting in normalization of liver biochemistries in 24, while 2 showed a significant clinical improvement, and 7 underwent liver transplantation or died. Remarkably, renal lesions in 6 patients resolved after CDCA treatment, or liver transplantation. There were no significant correlations between genotype and clinical outcomes.
Conclusions
In what is the largest cohort of patients with HSD3B7 deficiency thus far studied, renal lesions were a notable clinical feature of HSD3B7 deficiency and these were resolved with suppression of atypical bile acids by oral CDCA administration.

关键字 bile acid synthesis, chenodeoxycholic acid, genetic spectrum, HSD3B7, renal lesions, 3β-hydroxy-Δ5-C27-steroid oxidoreductase deficiency

分类：24. Rare Diseases 罕见病
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Prenatal diagnosis and early intervention improve neurodevelopmental and epileptic outcomes in children with tuberous sclerosis complex: a large retrospective cohort study

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Background: Epilepsy and intellectual disability are the greatest challenges and disease burden for children with TSC. Prenatal diagnosis offers the possibility of early intervention in TSC.
Method: This retrospective study was derived from a single-center TSC-specific cohort. We enrolled 273 individuals (including 31 with a fetal diagnosis) with definite TSC, completed TSC1/TSC2 genetic testing, and were followed up to at least 2 years of age.
Results: We compared prenatally diagnosed individuals (PreDI) with postnatally diagnosed individuals (PostDI), and prenatally diagnosed individuals with sirolimus and vigabatrin prophylactic intervention with non-intervention individuals in terms of epilepsy and neurodevelopment to assess the benefits of early attention and intervention. including. The rate of epilepsy occurrence was significantly lower in the PreDI group compared to the PostDI group (p=0.027). In the PreDI group, the rate of epilepsy in the subgroup given preventive treatment (38.9%, 7/18) was significantly lower than that of the subgroup not given preventive treatment (84.6%, 11/13) (p=0.008). The PreDI group showed significant improvements in cognitive, language, and motor development compared to the PostDI group and the preventive intervention group compared to the non-intervention group (p< 0.05).
Conclusions: Cardiac rhabdomyomas and/or intracranial lesions combined with TSC1/TSC2 genetic testing is a appropriate and effective method for prenatal diagnosis. Early postnatal interventions (sirolimus and vigabatrin) based on prenatal diagnosis can reduce the incidence of epilepsy and significantly improve neurodevelopmental outcomes.

关键字 TSC; prenatal diagnosis; neurodevelopment; epilepsy; child

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Genotype and phenotype in 28 Chinese patients with PLA2G6-related neurodegeneration

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Background: To report the clinical features and gene variants of 28 molecularly confirmed Chinese individuals with PLA2G6-related neurodegeneration.
Methods: We recruited 28 patients with molecularly confirmed PLA2G6-related neurodegeneration (PLNA) from 24 unrelated families in China, with two sick siblings in each four families. The detailed clinical features and gene variants of these 28 Chinese PLNA patients were reviewed.
Results: Among the 28 Chinese patients with PLA2G6 gene variants, 26 were diagnosed with INAD with the symptoms began at years of 6 months-3years of age. One patient was late-onset (6.5 years old) atypical NAD; another was diagnosed with Parkinson disease. 28.6% (8/28) of the patients had at least once seizures. Almost all INAD patients exhibited moderate to severe progressive psychomotor retardation. Other characteristics of 26 INAD patients include mental or cognitive retardation (26/26;100%), hypotonia (17/24;70.8%), hypertonia (7/24;29.2%), unable to walk (14/26;53.8%), walking with gait instability (12/26;46.2%), spastic tetraplegia (10/26;38.5%), autonomic involvement (11/22;50%), unable to speak (18/24;75%), simple language (6/24;25%), hearing impairment (3/26;11.5%), visual impairment (14/26;53.8%), nystagmus (13/26;50%), mode or behavor changes (5/15;33.3%), cerebellar atrophy (4/14;28.6%). Compound heterozygosity were found in 27 patients and homozygous mutaion in one INAD patient.
Conclusions: This report highlighted the phenotypic presentation of PLA2G6-related neurodegeneration in Chinese population.

关键字 PLA2G6 gene, Chinese, infantile neuroaxonal dystrophy, INAD, PLAN

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A novel heterozygous mutation in the FN1 gene causes thin basement membrane nephropathy: A case report

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Thin basement membrane nephropathy (TBMN), a common and lifelong condition, is pathologically characterized by glomerular basement membrane thinning accompanied by persistent hematuria. Similarly, glomerulopathy with fibronectin (FN) deposits (GFND) is also a kidney disease, that is characterized by fibronectin widely depositing in glomerulus, especially in the mesangial area and the subendothelial area. However, few studies have addressed the correlation on the two kidney diseases. This study is based on the clinical findings of a proband with TBMN, whose FN1 has a novel heterozygous mutation (c.3415G>A; p.V1139I). Summarizing the clinical phenotypes of the patient and interpreting the mechanism through renal biopsy pathological analysis and in vitro experiments, we aim to explore the pathogenic mechanism of TBMN from a genetic perspective.

关键字 thin basement membrane nephropathy; glomerulopathy with fibronectin deposits; FN1;heterozygous mutation

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Follow-up Analysis of Five Aromatic L-amino Acid Decarboxylase Deficiency Children in China

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Objectives: Aromatic L-amino acid decarboxylase deficiency (AADC) is a rare autosomal recessive neurometabolic disease. The clinical manifestations and prognosis of 5 children diagnosed with AADC in our hospital were analyzed, so as to improve the early recognition and intervention of the disease.
Methods: Clinical characteristics, laboratory examination, imaging and genetic characteristics of AADC patients diagnosed in department of Neurology, Children's Hospital of Fudan University from January 1, 2015 to December 31, 2020 were followed up and analyzed.
Results: (1) Baseline: male: female = 3:2; the average onset age of disease was 3m; the average diagnosis age by trio-WES was 19.8m. The mean follow-up time was 3.5y. (2) Clinical characteristics: 60% of the children had abnormalities in the neonatal period, including hypoglycemia, respiratory distress, and brain injury. All 5 patients had dystonia, such as fluff, poor head control ability, low trunk muscle tone and high limb muscle tone. All of them had movement lag (100%), which indicated that all of them were behind the developmental milestones. All patients had typical movemental crises (100%), with frequent attacks, once every 2-3 days, and clear consciousness. The attacks were manifested as body rigidity, antineotropy of the pedicles, oblique eyes, and tongue vomiting, lasting 2-4 hours. After the attack was relieved, drowsiness was observed without obvious myoclonus and tremor. All 5 cases had developmental delay, including motor, cognitive and language. All patients had ocular abnormalities (100%), including ptosis (3 cases) and poor gaze (4 cases). All patients had autonomic nervous disorder symptoms (100%), such as hypersweating, nasal congestion, salivation, unstable body temperature, laryngeal wheezing, etc. 80% of the children had feeding difficulties, including poor masticatory function, gastroesophageal reflux, and slow weight gain (all less than 3 standard deviations of the same age). (3) Physical examination: All the children had small hands and feet, soft body. (4) Laboratory examination: there were no obvious abnormalities in laboratory hematuria tandem mass spectrometry, but the peripheral blood dopamine, 5-hydroxytryptamine, adrenaline and norepinephrine were significantly lower than the lower limits. 3-O-methyldopa (3-OMD) on peripheral blood filter paper was significantly increased in 4 cases (>350ng/ml). (5) Imaging and EEG: non-specific changes (frontotemporal space widening, lateral ventricle fullness, insufficient brain volume, etc.) were found in 4 cases of head MRI, and only case 2 was normal. Two children had abnormal video-EEG, which showed abnormal background activity or epileptic discharge, and the rest were normal. (6) Genetic tests: through trio-WES detection, 4 cases had DDC compound heterozygous mutations, only case 3 had homozygous mutations, besides 4 cases had existed c. 714 + 4 A > T hot spot mutations, 2 cases of c. 106 g > A, HGMD database has been reported. (7) Drug therapy: All the 5 children received dopamine receptor agonists (pramexol orally, neuplo patch), monoamine oxidase inhibitors (selegiline) and vitamin B6, but the effect was poor. (8) Prognosis: 2 patients died, and the other 3 patients had daily movemental crises. Case 5 showed slight improvement in exercise ability due to the initiation of medication at the age of 11 months.

Conclusions: The disease started within 6 months of age in children with AADC, which was mainly characterized by dystonia, developmental delay, paroxysmal ankylsis, eye movement crisis and eye abnormalities. WES and blood 3-OMD tests of family members were helpful to make a definite diagnosis. Routine drug control was not satisfactory, and the prognosis was poor. However, early medication is expected to improve motor performance.

关键字 AADC, dystonia, developmental delay, paroxysmal ankylsis, eye movement crisis

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Neonatal Hyperekplexia with Two Novel GLRB Mutations: A case report and literature review

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Background: Hyperekplexia is a rare but treatable neurological disorder, characterized by excessive startle response to unexpected stimuli. It can show serious results, including apnea, bradycardia, aspiration pneumonia and sudden death in neonate. We report a neonatal patient whose frequent convulsions triggered by sudden noise or tactile stimuli.
Methods: DNA extraction, whole-exome sequencing analysis, and mutation analysis of GLRB were performed to obtain genetic data on the patient. We subsequently analyzed the patient's clinical and genetic data. Literature review of GLRB-mediated hyperekplexia was made.
Results: The patient's clinical manifestations were frequent episodes as sudden massive generalized body jerks triggered by loud noise or sudden touch and recurrent breath-holding attacks for 2 to 3 minutes, which was diagnosed as neonatal hyperekplexia. Two novel compound heterozygous GLRB mutations at c.527G>A(p.Val1282del) and c844-846delGTT(p.Arg176Lya) were detected.
Conclusion: Our report reveals a neonate case illustrating the characteristics of hyperekplexia induced by GLRB gene mutation. Our findings expand the mutant spectrum of the GLRB gene and contribute to the refinement of the genotype－phenotype mapping of hyperekplexia. Awareness of this disease will avoid misdiagnosis in neonates and lead to a timely treatment. Molecular genetic screening for diagnosing hyperekplexia is valuable.

关键字 hyperekplexia; excessive startle response; GLRB gene; WES

分类：24. Rare Diseases 罕见病
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Genotypes and phenotypes of DNM1 variants related developemental and epileptic encephalopathy

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【Abstract】Background The DNM1 gene is mapped to chromosome 9q34 (OMIM:601011), it encodes dynamin-1, a GTP ase that has a critical role in synaptic vesicle recycling in the brain, particularly during postnatal development. In this study, we summarize the genotypes and clinical features of epilepsy children with DNM1 gene variants. Methods The genotypes and clinical features of thirteen children with DNM1 variants in the pediatrics department of Peking University First Hospital were analyzed. Results There were 6 boys and 7 girls. The age of seizure onset ranged from 15 days after birth to one year old and 10 months, the median age was 6 months. There were 12 missense variants, 1 frameshift variant. 13 variants were de novo. Multiple seizure types were observed, including epileptic spasms in 13 patiets, focal seizure in 8 patients, atypical absence seizure in 2 patients and tonic seizure in 2 patients. All 13 patients showed varied degree of development delay. Three patients had slow rhythm of background activity. The electroencephalography showed hypsarrhythmia in 10 patients. Epileptic spasms was captured in 6 patients, tonic seizure was captured in one patients and non-convulsion status epilepticus was captured in one patient. Brain magnetic resonance imaging (MRI) showed the frontotemporal subarachnoid space widened in 5 patients, corpus callosum dysplasia in 1 patients, cerebral atrophy in 2 patients. The age of the last follow-up ranged from 1 year old and 2 months to 7 years old. After multi-drug treatment, 2 patients were seizure free, one patient died of severe pneumonia at age 2, 10 patients still had intermittent seizures, The clinical phenotype of one patient was transformed from infantile spasm to Lennox-Gastaut syndrome. Conclusion The seizure onset age of epilepsy caused by DNM1 gene mutation usually begins in infantile period. The main types of seizures were epileptic spasms and focal seizures. Often there are varying degrees of developmental delay, which can occur before seizures. The clinical manifestations are mostly infantile spasm syndrome, and some children can be transformed into Lennox-Gastaut syndrome. Epilepsy caused by DNM1 gene mutation is mostly drug-resistant epilepsy.

关键字 DNM1, gene, Developemental and epileptic encephalopathy, infantile spasm syndrome

分类：24. Rare Diseases 罕见病
1385

Biotin thiamine reactive basal ganglia with infantile spasm as the first manifestation: a family report

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Objective: We retrospectively analyze a case of biotin thiamine reactive basal ganglia disease in a family with infantile onset and infantile spasm as the first manifestation, summarize the clinical characteristics and review the literature.
Methods: The clinical data and molecular genetic test results of a family with biotin thiamine reactive basal ganglia disease were analyzed retrospectively, and the relevant literature was analyzed.
Results: case 1: A girl appeared drowsiness at the age of 1 month after birth, Spasm seizure was found at the age of 3 months, which was diagnosed as "infantile spasm". Cranial MRI and gene were not checked, and no treatment was given. She died at the age of 4 months. Case 2: the sister of case 1, who developed at the age of 1 month, showed drowsiness and poor appetite. Paroxysmal limb shaking occurred at the age of 3 months, oral "levetiracetam oral liquid", and paroxysmal nodding occurred at the age of 5 months. EEG examination at the age of 6 months: multiple spasms were recorded in the awake period, and the background was highly irregular. She was diagnosed as "infantile spasm". Cranial MRI showed abnormal symmetrical signals in bilateral frontoparietal junction, basal ganglia, thalamus, midbrain, brain foot and brain stem. Homozygous mutation of SLC19A3 gene in children was found by whole exon gene sequencing (WES): C. 437_ 438insgt (P. t147sfs * 62), the mutation comes from parents, resulting in frame shift mutation of amino acids. Bioinformatics analysis suggested suspected pathogenic variation. No abnormality was found in mitochondrial gene. The patient was finally diagnosed as biotin thiamine reactive basal ganglia disease (BTBGD). She was treated with biotin, thiamine and "cocktail therapy", Antipiletic drugs were given containing levetiracetam, ACTH, topiramate, aminohexenoic acid and sodium valproatem in sequence. After case 2 was confirmed, case 1 was verified to have the same gene mutation site, which was homozygous mutation in SLC19A3 gene: C. 437_ 438insGT(p. T147Sfs*62)。
Conclusion: Biotin thiamine reactive basal ganglia is a treatable autosomal recessive disease. The main clinical manifestations are dysarthria, seizures and subacute encephalopathy. Infants with onset and infantile spasm as the first manifestation have characteristic neuroimaging manifestations. It is necessary to be vigilant against biotin thiamine reactive basal ganglia disease and give biotin, thiamine and "cocktail therapy" as soon as possible. The genetic diagnosis of proband is helpful to make a clear diagnosis and give birth to good children.

关键字 biotin reactive basal ganglia disease , SLC19A3 , gene infantile spasm

分类：24. Rare Diseases 罕见病
1395

Herpes simplex encephalitis triggerded epileptic spasms and EEG Abnormalities in an Infant With West Syndrome and Anti-NMDAR Encephalitis: a case report

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A 4-month-old infant was admitted to the hospital due to seizure-like movements for 3 months. She had eaten less and fever at 27 days after birth. Her cerebrospinal fluid protein increased (537-1402) mg/L, cerebrospinal fluid sugar decreased (1.72-2.64) mmol/L, high-throughput examination of blood and cerebrospinal fluid showed herpes simplex virus type I infection, high-throughput examination of cerebrospinal fluid revealed fungal sequence. Two weeks later, she had seizure-like movements appeared before going to bed. Video EEG showed high arrhythmia, isolated or series of seizures were detected. Head MRI displaced extensive encephalomalacia and brain atrophy in both cerebral hemispheres, cortical necrosis and "empty brain"-like morphological changes, bilateral basal ganglia, cyst hindlimbs and dorsal thalamus, thinning of the corpus callosum, and less white matter adjacent to the ventricles. Both sides of the ventricle and the third ventricle are dilated, and the above-mentioned changes are considered after brain injury. Anti-NMDAR antibody encephalitis was diagnosed with cerebrospinal fluid anti-NMDAR antibody 1:3.2, and seizures were reduced by applying methylprednisolone 150mg pulse therapy.

关键字 Anti-NMDAR Encephalitis， Herpes simplex encephalitis， spasms，EEG

分类：24. Rare Diseases 罕见病
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Wiedemann-Steiner Syndrome: a novel missense mutation in KMT2A and review of literature

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Wiedemann-Steiner syndrome (WDSTS) is a rare genetic disorder characterized by intellectual disability, short stature and dysmorphic facial appearances in general. In 2012, Jones et al identified heterozygous mutations in KMT2A (lysine methyltransferase 2A) as the molecular cause of WDSTS.
Although the phenotype of this syndrome continues to expand, the relationship between clinical features and genes are not fully understood. Here, we report one Chinese girl with a novel nonsense KMT2A mutations. She had serious growth deviation and cleft palate , which was not been previously reported in WDSTS. Exome sequencing analysis of thepatient and their parents revealed a de novo nonsense mutation, c.901C>T (p.R301 X) on KMT2A, which molecularly confirmed the diagnosis of Wiedemann-Steiner syndrome. In addition, we summarized the clinical features of WDSTS associated with KMT2A mutation and discussed the cardinal symptoms in detail.

关键字 Growth deviation; KMT2A; Wiedemann-Steiner syndrome

分类：24. Rare Diseases 罕见病
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Duplication 9p Syndrome: a de novo duplication in the p13.1-24.3 of chromosome 9 in a Chinese girl：A case report and literature review

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Background: Duplication 9p syndrome is a well-described chromosomal disorder, which can affect either a part or the whole short arm of chromosome 9. The patients with this syndrome mainly manifests as developmental delay and craniofacial anomalies, some of whom may accompanied by hypotonia and limb abnormalities. Since the first case reported by Rethore´ et al in 1970, in excess of 200 patients have been reported till now. But the isolated duplications of 9p without concurrent deletions was reported only in a few papers.
Case presentation: We report here on a new patient with partial trisomy 9p13.1-p24.3 in a 6-year-old girl with speech / language and motor delay, short stature, and distinctive facial features that were strikingly similar to those previous related cases.
Methods：Whole exome sequencing (WES) , Chromosomal microarray (CMA) and Copy Number Variation (CNV) was performed on proband.
Results: Cytogenetics indicated that our proband karyotype was 46,XX,add(12)(q?). Copy number variation by shotgun sequencing revealed a 39.82 Mb duplication in the p13.1-p24.3 region of chromosome 9.
Conclusion: Combination of both the clinical manifestation and genetic tests, we conclude that this pathogenic copy number variation could explain the phenotype of our patients. This de novo duplication in the p13.1-p24.3 region of chromosome 9, which advances our understanding of 9p duplication syndrome, and diversifies the cases reported for this condition.

关键字 duplication 9p syndrome, developmental delay, copy number variation.

Category: 24. Rare Diseases 罕见病
1450

Radiographic Changes and Long Term Outcome of a Patient with Severe Infantile Hypophosphatasia

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Abstract Content Hypophosphatasia (HPP) is a rare metabolic bone disease caused by loss of function mutations in the ALPL gene (OMIM 171760), which encodes tissue-nonspecific alkaline phosphatase (TNSALP). This is a phenotypically heterogenous disorder and classified into six forms based on the age of onset and severity. There is no clear genotype-phenotype correlation. Enzyme replacement therapy (ERT) using bone-targeted recombinant alkaline phosphatase (ALP) such as asfotase alfa led to improvement in the prognosis of patients with life-threatening HPP. We illustrate the natural history and unique skeletal findings of a girl with infantile hypophosphatasia (OMIM 241500) on six years follow up who did not receive ERT.

Methods We report on the clinical history, examination findings of a patient with confirmed infantile hypophosphatasia over a 6-year period. A 6-year-7-month-old girl who presented at one month old with failure to thrive, hypercalcaemia and respiratory failure was reviewed. Physical examination revealed a girl with short stature, appropriate head size and rhizomelic limb shortening and deformities. There was bell-shaped chest and poor dentition. Biochemical changes included low serum ALP, elevated urine phosphoethanolamine (PEA) and serum pyridoxine level. Typical skeletal findings with hypomineralization and metaphyseal changes. The diagnosis of infantile HPP was supported by the findings of compound heterozygous mutation in ALPL gene: c707 A>G and c928-929delTC, which were likely pathogenic variants. Both parents were carriers. Her ongoing health difficulties include restrictive lung disease required non-invasive ventilator support, gross motor delay, growth failure with food aversion and poor dentition.

Results The natural course of disease and serial radiographic changes for severe infantile HPP in an Asian child who did not receive ERT were described. There is a need to understand the long-term natural history and progression of rare diseases such as HPP. In our patient, the prognosis was initially assessed to be guarded due to the severe presentation. However, the patient gradually improved with supportive treatment. While ERT for severe HPP improved the survival rate and skeletal complications, it is not routinely available especially in low resource settings and countries. Hence genetic counselling, supportive treatment and multidisciplinary management remain the mainstay of long-term care. Efforts to make ERT accessible to all patients with HPP must be made.

Conclusion Rare diseases such as infantile hypophosphatasia must be given attention and research in low- and middle-income countries. This is to ensure equitable access to care and treatment for patients to prevent complications and disabilities

Key words rare disease, developing countries, natural history, hypophosphatasia
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分类：24. Rare Diseases 罕见病
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Updated clinical and glycomic features of mannosyl-oligosaccharide glucosidase deficiency (MOGS-CDG)

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Background Mannosyl-oligosaccharide glucosidase (MOGS) deficiency is an extremely rare type of congenital disorders of glycosylation (CDG) with only twelve reported cases, and reported features are still expanding.

Aims Our objective is to update clinical and glycosylation features of two patients with MOGS-CDG that have been previously reported without solid functional or glycomic evidence.

Methods We collected comprehensive clinical information, and conducted glycosylation study with IgG1 assay using nano-electrospray ionization source quadruple time-of-flight (Nano-ESI-Q-TOF) method.

Results Novel dysmorphic features include enlarged tongue, forwardly rotated earlobes, a birth mark, overlapped toes, and abnormal fat distribution. Novel imaging findings include pericardial effusion, deep interarytenoid groove, mild congenital subglottic stenosis, and laryngomalacia. Novel laboratory findings include peripheral leukocytosis with neutrophil predominance, elevated C-reactive protein, elevations of creatine kinase, dyslipidemia, coagulopathy, complement 3 and complement 4 deficiencies, decreased proportions of T lymphocytes and natural killer cells, and increased level of serum interleukin-6 levels. Glycosylation studies showed significant increase of hypermannosylated glycopeptides (Glc3Man7GlcNAc2/N2H10 and Man5GlcNAc2/N2H5) and significant increase of hypersialylated glycopeptides. A compensatory glycosylation pathway leading to increase of Man5GlcNAc2/N2H5 was indicated with the glycosylation profile.

Conclusion We confirmed abnormal glycomics in one patient, expanded clinical and glycomic spectrum in MOGS-CDG, and postulated a compensatory glycosylation pathway in leading to a possible serum biomarker for future diagnosis.

关键字 Mannosyl-oligosaccharide glucosidase; MOGS-CDG; Congenital disorders of glycosylation type IIb; MOGS gene; Glycomics of IgG1

分类：24. Rare Diseases 罕见病
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TMEM199-CDG masquerading as Wilson disease

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Background and objective: TMEM199-congenital disorder of glycosylation (TMEM199-CDG) is a rare autosomal recessive disorder characterized by chronically elevated serum transaminases and alkaline phosphatase, decreasedserum ceruloplasmin, steatosis and/or fibrosis, TMEM199 gene mutation, reduced function of transmembrane protein 199 protein, and abnormal protein glycosylation. We report a new patient with TMEM199-CDG who previously diagnosed and treated as Wilson disease.

Methods: Clinical, histopathological, and molecular features of a Han Chinese boy with TMEM199-CDG treated in the Children’s Hospital of Fudan University were reviewed.

Results: The 4-years-old Han Chinese boy presented with hypertransaminasemia, hypercholesterolemia, elevated alkaline phosphatase, decreased serum ceruloplasmin, reduced serum copper level, elevated alpha-fetoprotein levels, and coagulopathy. He was previously diagnosed as having Wilson disease and treated with copper chelator with no improvement. He was referred to our center after genetic testing revealed no mutation ATP7B gene, and compound heterozygous mutations in TMEM199 gene. A known disease-causing missense mutation inherited from his healthy father, and a novel frameshift mutation leading to a truncated protein inherited from his healthy mother. Other findings include strabismus, allergy, cirrhosis with ductal plate malformation in liver biopsy, reduced expression of TMEM199 protein in liver tissue. Oral administration of ursodeoxycholic acid and D-galactose led to improved liver function test results.

Conclusion: This report not only adds to the phenotypic and genotypic spectrum of TMEM199-CDG, but also indicates ursodeoxycholic acid and D-galactose as possibly effective treatment options. TMEM199-CDG should be considered when the diagnosis of Wilson disease was questioned by genetic testing and treatment response.

关键字 Congenital disorders of glycosylation; Transmembrane protein 199; TMEM199-CDG; Wilson disease; TMEM199 deficiency;

分类：24. Rare Diseases 罕见病
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Congenital disorders of glycosylation and deglycosylation in China: 51 unreported cases, current status, and future perspectives

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Background and Objective: Congenital disorders of glycosylation (CDG) and deglycosylation (CDDG) are a rapidly growing group of diseases. Reports from mainland China are mainly restricted to case reports or small case series, and large-scale data is lacking. Our objective is to present clinical phenotypes of 51Chinese children with various CDGs, review current status of research in mainland China, and provide future perspectives to improve patient care.

Method: We searched electronic medical records from Jan 2009 to July 2019 in the Children's Hospital of Fudan University and collected all patients suspected to have congenital disorders glycosylation on the basis of clinical phenotype and genetic testing. We also searched for additional patients reported during past 10 years from mainland China in Chinese language medical literature database (CNKI, China Knowledge Resource Integrated Database, http://new.oversea.cnki.net/index/; and Wanfang Database, http://www.wanfangdata.com). The following inclusion criteria is applied for patient selection: (1) Patients with deleterious or known disease-causing mutations in CDG related genes compatible with inheritance mode of the specific gene; (2) Patients carrying variants of unknown significance (VUS) and have evidence of a glycosylation defect or functional deficiency of the gene product.

Results: We found 5 cases of ALG1-CDG with 1 novel frameshift mutation, 2 cases of ALG13-CDG, 2 cases of ATP6Ap1-CDG, 1 case of CCDC115-CDG with 1 novel frameshift mutation and 1 novel exon deletion, 2 cases of COG4-CDG with 1 novel truncating mutation, 1 case of COG5-CDG with 1 novel canonical splice-site mutation, 5 cases of MAGT1-CDG with 4 novel deleterious mutations, 3 cases of MPI-CDG with 1 novel in-frame insertion, 5 cases of NGLY1-CDDG with 4 novel nonsense mutations, 1 case of PGM1-CDG, 18 cases of PMM2-CDG with 3 novel truncating mutations, 3 cases of SLC35A2-CDG with 2novel frameshift mutations, 1 case of SRD5A3-CDG with 1 novel nonsense mutation, 1 case of SSR4-CDG with 1 novel nonsense mutation, and 1 case of TMEM199-CDG with 1 novel frameshift mutation. We also pointed out novel phenotypical findings in each CDG category within our patient cohort. English literature search showed that CDG/CDDG research in mainland China is mainly limited to case reports and small-scale case series, and large-scale studies are lacking. Although genetic testing is becoming popular in China, there is an urgent need to establish routine CDG screening by clinical glycomics tools for definitive diagnosis and treatment monitoring.

Conclusion: We expanded clinical phenotype and genetic mutation spectrum of congenital disorders of glycosylation by reporting 51 cases with 15 types of CDG, and 21 novel deleterious mutations from mainland China. We also reviewed current status of CDG and CDDG research in China and pointed out further research directions to improve patient outcomes.

关键字 CDG; Congenital disorders of glycosylation; CDDG; Congenital disorder of deglycosylation; mainland China; Phenotype; Genotype;

分类：24. Rare Diseases 罕见病
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Fanconi－Bickel Syndrome in an infant patient with With Severe Hypokalemia

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Fanconi－Bickel syndrome (FBS) is a rare autosomal recessive disease affecting carbohydrate metabolism and can lead to glycogen accumulation in the kidney and liver. Solute carrier family 2 member 2 (SLC2A2) encodes a protein that regulates bidirectional glucose transport and previously has been associated with FBS. Here we report a clinical case of a 6-month-old girl with severe hypokalemia, the other typical symptoms included abnormal blood electrolytes, liver function, and glucose. Her family history is significant for consanguineous parents. Whole exome sequencing revealed a truncating mutation (NM_000340.2; p. Trp420*) of SLC2A2 in our patient. In this report, we present a novel SLC2A2 mutation responsible for FBS and associated phenotype.

关键字 SLC2A2, GLUT2, Fanconi－Bickel syndrome, Hyperglycemia, Hypokalemia

分类：24. Rare Diseases 罕见病
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The effectiveness of tofacitinib in Blau syndrome: A case series of Chinese pediatric patients

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Objective：Blau syndrome (BS), a rare and autosomal-dominant autoinflammatory syndrome, is characterized by the syndromes of granulomatous recurrent uveitis, dermatitis, and symmetric arthritis. It is associated with mutations of the nucleotide-binding oligomerization domain containing 2 (NOD2) gene. Therefore, the missense heterozygous mutation in NOD2 gene could cause an activation of NF-κB that could lead to the secretion of the pro-inflammatory cytokines like IL-1β, IL-6 and TNF-α. While, the biologic agent such as tocilizumab, a Janus kinase (JAK) inhibitor, has a promising performance in preventing inflammatory cytokines from increasing in rheumatoid arthritis patients. However, whether tofacitinib has a similar effectiveness in BS, especially in child patients is not clear. So our aim of this study is to assess the efficacy of tofacitinib in Chinese child patients with BS.
Methods：Tofacitinib was regularly given to thee BS patients (termed as Patient-1, -2, and -3) in different dosage: 1.7 mg/day (0.11 mg/kg), 2.5 mg/day (0.12 mg/kg), and 2.5 mg/day (0.33 mg/kg), respectively. The clinical manifestations of patients, magnetic resonance imaging, serological diagnosis, and therapeutic measures and outcomes of treatments were recorded in the end. The inflammatory cytokines (IL-1β, IL-2, IL-4, IL-6, IL-10, TNF-α, IFN-γ) were measured by ELISA assay.
Results：The clinical characteristics and serological diagnosis of all BS patients were drastically improved after they received tofacitinib treatment such as the relieved joint pain and swelling. All mutations were located on exon 4 of the NOD2 gene in these patients, and a novel unreported mutation (p.M513K) in NOD2 was found in Patient-3. All the patients have reached clinical remission of polyarthritis and improvements in erythrocyte sedimentation rate, levels of C-reactive protein and inflammatory cytokines after 12 month treatment with tofacitinib. Most importantly, no side effects were seen during tofacitinib treatments.
Conclusion：The improvement of inflammatory symptoms in BS suggests that tofacitinib treatment is a promising and effective therapeutic approach for BS patients who have an unsatisfactory response to the corticosteroids, biological reagents and traditional disease-modifying antirheumatic drugs like methotrexate, tocilizumab and etanercept.

关键字 Blau syndrome，tofacitinib，pediatric patients，inflammatory cytokines

分类：24. Rare Diseases 罕见病
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A case of non-AIDS child with Penicillium marneffei pneumonia with heterozygous mutation of STAT3

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Introduction: Talaromyces marneffei (TM) infection is rarely seen in clinical practice, and its pathogenesis may be related to deficiency in antifungal immune function. signal transducer and activator of transcription 3 (STAT3) is a key molecule in fungal immune surveillance. There have been no previous case reports of TM infection in individuals with STAT3 gene mutations. Herein, we present a very rarely reported case of Talaromyces marneffei infection with a STAT3 gene mutation
Presentation of case: Our patient was a 11-month-old Chinese girl who was admitted to our hospital with repeated cough and asthma for 3 months, and a hoarse voice for 3 days. Metagenomic next-generation sequencing (mNGS) of BALF sample confirmed TM infection. The pathological examination results of BALF samples also suggested TM infection. Whole exome sequencing revealed that the patient had a c.1394C>T variation in exon16, Causing amino acid No. 465 to change from serine to phenylalanine (p.S465F). Based on the culture results, amphotericin B antifungal therapy was administered. After the administration on the 4th day, the patient's hoarseness improved significantly, and the symptoms of cough and asthma were alleviated significantly.After 2 weeks of intravenous amphotericin B, we changed to oral sequential treatment with voriconazole. Two months later, the patient's lung CT was significantly better than before, and the antifungal drugs are still being taken orally.
Conclusion: This is the first report on Talaromyces marneffei (TM) infection in a child with a STAT3 gene mutation. Unexplained TM infection in HIV negative individuals warrants investigation for immune deficiencies.

关键字 immunodeficiency disease; STAT3 mutation; Talaromyces marneffei infection; fungal immunodeficiency; STAT3 deficiency,

分类：24. Rare Diseases 罕见病
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Familial episodic pain syndrome-2: Case reports and Literature review

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Background: Familial episodic pain syndrome-2 is a rare, genetic, peripheral neuropathy disorder characterized by episodic pain of extremities. Due to its mimicking of arthralgia, it is always underestimated.
Method: We reported 3 cases of clinically diagnosed familial episodic pain syndrome-2(FEPS-2) to discuss the clinical characteristic of FEPS-2 and to raise awareness of the pain syndrome among the clinicians. We retrospectively collected and summarized three patients clinically diagnosed and highly suspected diagnosed with familial episodic pain syndrome-2.
Results: We included 3 cases. Case 1 is an eight-year-old boy, he manifested episodic paraesthesia of the lower extremities, with burning sensation and swelling. Still, he didn’t have any swollen joints and limitations of motion. No positive family history was observed in his family. The whole exon study confirmed a heterozygous variant of SCN10A (c.1114_1115insA), indicating the diagnosis of Familial episodic pain syndrome type 2. Case 2 is a 13 years old boy who manifested plantar pain with no painful and swollen joint. Several relatives on the patient’s maternal side, including the boy’s mother, uncle, aunty, grandmother, have similar symptoms. The whole exon sequencing identified a heterozygous variant of SCN10A (c.2869A>T). Case 3 is a 13 years old girl who showed arthralgia with no swelling and limitation of motion. Likewise, the girl’s mother and grandmother showed similar symptoms. Familial episodic pain syndrome-2 is a rare, genetic, peripheral neuropathy disorder characterized by recurrent, episodic intense pain, predominantly involving the lower extremities. The painful sensation can be triggered or exacerbated by fatigue, cold exposure, weather changes, or physical stress. In addition, sweating and other manifestations, such as tachycardia, breathing difficulties, and generalized pallor, may be associated. Faber et al. have first identified the causative gene of SCN10A responsible for FEPS-2. By searching the ClinVar database to date, we have found 790 variants, most of which are responsible for the Brugada syndrome. Only 19 variants are associated with the phenotype of familial episodic pain syndrome-2. Of note, the variant rs6801957 of SCN10A is related to human mechanical pain sensitivity.
Conclusion: In conclusion, we highly recommend genetic sequencing among patients with arthralgia and pain syndrome.

关键字 genetic, episodic pain

分类：24. Rare Diseases 罕见病
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The mechanism of Automatic brewery syndrome induced by intestinal dysbiosis

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Background Auto-brewery syndrome (ABS) describe a condition in which patients become inebriated after the ingestion of an alcohol-free, heavy carbohydrate diet. The first case of ABS reported was a 5-year-old African boy in 1948. We have previously demonstrated that *Klebsiella* with high ability for producing endogenous ethanol is one of potential causes of ABS. However, because there are limit of cases of ABS, it is necessary to seek further evidence to support this concept in clinic.
Methods An ABS patient, who suffered with repeated bouts of unexplained intoxication without alcohol consuming for nine years. Next generation sequencing was used to characterize the intestinal flora of this ABS patient in different stages. An in vitro fermentation system was used to cultivate samples for sensitive drug screening and inducing factors. Mouse model was established to verify that the isolated strains could induce ABS in vivo.
Results The distribution Proteobacteria in fecal samples strongly correlated with fluctuations of the patient blood alcohol concentration and the abundance of genus *Klebsiella* was significantly increased during the morbid states. Treating the patient with low-carbohydrate diet and levofloxacin resulted in the alleviation of ABS and no further recurrence of symptoms. All three strains of high-alcohol producing *Klebsiella* isolated from the patient were able to induce ABS in mice, while monosaccharides might be the major food-induced factors.
Conclusion We extended and confirmed our previous findings through another clinic case of ABS, further demonstrating that proper antibiotics plus controlled diet was able to benefit for treatment of bacterial derived ABS. Our data will help clinicians for precisely diagnosis and alternative therapeutics for ABS in the future.

关键字 Auto-brewery syndrome, Klebsiella, Diagnosis, Treatment

Clinical Pharmacology

临床药理

分类：6. Clinical Pharmacology 临床药理
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Identification of Predominant CC59-SCCmec IV-agr I with Low Vancomycin Minimum Inhibitory Concentration in MRSA Isolated at a Chinese Children's Hospital between 2010 and 2019

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Objectives: Elevated vancomycin minimum inhibitory concentration (MIC) in Staphylococcus aureus (S. aureus) has been associated with worse clinical outcomes. This study aimed to investigate the change trend of vancomycin MICs and assess the relationship of this characteristic with genetic background using methicillin-resistant S. aureus (MRSA) strains isolated from Chinese children.
Methods: MRSA isolates were collected from Beijing Children's Hospital from 2010 to 2019 and positively identified. Vancomycin susceptibility was tested by the broth microdilution (BMD) method. The multilocus sequence and staphylococcal cassette chromosome mec (SCCmec) and accessory gene regulator (agr) typing were determined by PCR.
Results: A total of 332 MRSA isolates were included in this study. The geometric mean MICs in 2010, 2012, 2013, 2016, 2017, 2018, and 2019 were 0.724, 0.767, 0.734, 0.763, 0.828, 0.719, and 0.762 mg/L, respectively. All isolates were susceptible to vancomycin. We observed that vancomycin MICs shifted over the course of the study; the proportion of isolates with a vancomycin MIC of ≥1 mg/L fluctuated at 6.5% in period I, 17.9% in period II, and 4.7% in period III. Combined analysis revealed that clonal complex (CC) 59-SCCmec IV-agr I is the most prevalent genotype (179, 53.9%). Compared with other genotypes, this complex was associated with lower rate of vancomycin MICs of ≥1 mg/L (P = 0.001).
Conclusions: Vancomycin MICs for MRSA isolates were shifting during the study period. The predominant clone CC59-SCCmec IV-agr I was associated with low vancomycin MICs.

关键字 CC59; Chinese children; MIC; MRSA; vancomycin

分类：6. Clinical Pharmacology 临床药理
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Cardiotoxicity in biological agent targeted therapy for rheumatoid arthritis: ADR Signal Mining and Analysis of FDA Adverse Event Reporting System Database

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Purpose: Biologic agent-induced cardiotoxicity is markedly concerning. Rheumatoid arthritis (RA) treated with biologic agents is known to have the potential for cardiotoxicity; however, existing clinical evidence is not adequate to explain real-world patterns of cardiotoxicity. In this study, we quantify the risk of cardiotoxicity in patients with rheumatoid arthritis treated with biological agents.
Methods: Cardiotoxicity reports induced by four types of biologic agents, abatacept, adalimumab, tocilizumab, and etanercept were used to mine data from the FDA's adverse event reporting system (FAERS) database from January 1, 2004 through September 30, 2020. Reports of cardiotoxic events were analyzed using a reporting odds ratio (ROR) algorithm, the proportional reporting ratio (PRR), the Bayesian confidence propagation neural network (BCPNN), the multi-item gamma Poisson shrinker (MGPS), and logistic regression methods. We use the preferred term of the Medical Dictionary of Regulatory Activities to identify such events.
Results: A total of 3,969 reports of cardiotoxic events were identifified involving biologic agents used for RA as the suspect drugs in this study, 317 reports of abatacept, 2,137 reports of adalimumab, 273 reports of tocilizumab, and 1,242 reports of etanercept. Adalimumab was the most reported, followed by etanercept. The proportion of death and disability outcomes reported for each targeted treatment represents approximately 20–25% of the total reported severe adverse events. In addition, relatively low cardiotoxicity reporting rates were found with abatacept.
Conclusion: Analysis of FAERS data offers a more precise profifile on the characteristics and occurrences of cardiotoxic events. The fifindings are a clinical reminder to physicians that an increased vigilance concerning the cardiotoxic effects of biological agents needs to be implemented. Also, more comparative studies are required in the future to explain the mechanisms that cause these cardiac phenomena.

关键字 biologics, pharmacoepidemiology, rheumatoid arthritis, adverse, drug-induced cardiotoxicity

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Pattern of antibiotic prescriptions in Chinese children, based on multi-center Point Prevalence Survey

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Background: Broad spectrum antibiotics have a potentially greater influence on antimicrobial resistance. In the current study, we describe the pattern of antibiotic prescriptions for children from 2017 to 2019 after the implementation of the National Special Rectification Activities on Clinical Antibiotic Use in 2011 based on the Anatomical Therapeutic Chemical Classification(ATC classification), the World Health Organization's (WHO) Essential Medicines List Access, Watch, and Reserve(AWaRe) classification and the Management of Antibiotic Classification in China.
Methods: One-day point-prevalence surveys (PPSs) on antimicrobial prescribing were conducted in hospitalized children in China in September 1st and November 30, once every year from 2017 to 2019.
Results: A total of 5060 antibiotic prescriptions for children were included in the analysis. There were 76 types of antibiotic agents in total, and 22 (28.95%) antibiotic agents accounted for 90 percent of antibiotic prescriptions. The top-five antibiotics prescribed for children were azithromycin(13.70%), ceftriaxone(10.32%), latamoxef(7.96%), Cefoperazone/Sulbactam(6.78%) and Meropenem(5.73%).
On the basis of WHO AWaRe classification, there were 42(55.26%) antibiotic agents in the Watch group, accounting for 76.15% of antibiotic prescriptions. There were three (3.95%) antibiotic agents in the not-recommended group, accounting for 8.34% of antibiotic prescriptions. According to the Management of Antibiotic Classification in China, there were 24(31.17%) types of antibiotic agents in the restricted group, accounting for 54.64% of antibiotic prescriptions. There were eight (10.39%) types of antibiotic agents in the special group, accounting for 13.04% of antibiotic prescriptions.
Conclusion: The proportion of the Watch group basing on AWaRe classification and the special group basing on the Management of Antibiotic Classification in China was high. It was probable that the broad-spectrum antibiotics overused in children in China.

关键字 Antibiotic; Children; Antibiotic stewardship; WHO Essential Medicines list for children; China;

分类：6. Clinical Pharmacology 临床药理
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Application of adrenocorticotropic hormone in recurrent focal segmental glomerulosclerosis post-transplantation: a case report and review of the literature

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Background: The recurrence rate of focal segmental glomerulosclerosis (FSGS) post-renal transplantation is as high as 30% to 50%. However, the pathogenesis is unclear. At present, there is no unified standard for the treatment of recurrent FSGS post-transplantation. Its treatment is full of risks and challenges.
Methods: We report a child with recurrent FSGS with massive proteinuria (6~9g/24-h) and resistance to plasma exchange (PE) and rituximab (RTX). On the basis of receiving anti-rejection therapy of prednisone, tacrolimus, and mycophenolate mofetil (MMF), we treated the child with adrenocorticotropic hormone (ACTH), and reviewed the literature on the application of ACTH in the recurrence of FSGS post-transplantation.
Results: After one year of treatment with ACTH, the patient's urinary protein decreased and fluctuated between 0.6~1.1g/24-h. The albumin (ALB) and cholesterol (CHOL) returned to the normal range. The patient achieved complete remission after nineteen months of ACTH treatment and maintained until now. There was no obvious adverse reaction. Literature review showed that up to February 2021, a total of 8 studies showed the use of ACTH in kidney transplant patients, and all the patients in the study achieved remission.
Conclusions: ACTH is a potential option for treating recurrent FSGS post-transplantation with fewer side effects and relatively safe for patients. However, further evaluation is needed to better adapt to different populations.

关键字 adrenocorticotropic hormone,focal segmental glomerulosclerosis

分类：6. Clinical Pharmacology 临床药理
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LC-MS/MS method for rapid determination perampanel concentration in plasma and its application in Chinese children with epilepsy: Be aware of potential drug-drug interactions

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Purpose: Perampanel (PER) is the first clinically available α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptor antagonist. Clinical studies have confirmed the relationship between dose-exposure-response-adverse reaction correlation. Owing to the high binding to plasma proteins, mainly metabolized by CYP3A4 and prone to drug interactions of PER, it is necessary to conduct therapeutic drug monitoring (TDM) for PER. In this study, we hope to develop a simple, fast, and suitable TDM method for the analysis of PER in children with epilepsy.
Method: In this study, perampanel-d5 was used as the internal standard (IS) and plasma samples were prepared by simple protein precipitation method with acetonitrile. The analyte was separated using a Kinetex C18 column (2.1 mm × 50 mm, 5 μm; Phenomenex) with a isocratic elution that the flow rate was 0.35 mL/min, and mobile phases were aqueous water containing 0.2 mM formic acid and 0.2 mM formic acid in acetonitrile (50:50, v:v). Detection was performed under positive electrospray ion (ESI) multiple reaction monitoring (MRM) mode through the m/z 350.3 → 219.1 and m/z 355.3 → 220.0 transitions for PER and the IS, respectively. According to the FDA bioanalytical method validation guidance (May 2018), the method was validated fully in term of selectivity, accuracy, precision, matrix effect, recovery, stability, and carryover. The hemolyzed and lipemic matrix effect were also investigated. Finally, this method was applied in clinical TDM on children with PER treatment.
Results: The lower limit of quantification was 1.00 ng/mL. The standard curve was linear Within in the range of 1.00-2000 ng/mL, (r = 0.9975). The intra- and inter-batch accuracy (Bias%: -5.6% - 8.0%) and precision (CV% ≤ 9.6%) between three consecutive analysis batches meet the criteria. The average extraction recovery of the analyte was 99.2%. The average IS-normalized matrix effect was 100.0%. The analyte was stable when placed samples at room temperature for 15 hours, 4° C autosampler for 6 days, -20° C freeze-thaw cycles for five times, and -20° C for one month. No obvious carryover effect was observed. Hemolyzed and lipemic matrix have no interference to the method. This method was applied to detect the PER concentration of 11 children with epilepsy. Ages of these children were ranged from10 months to 13 years old. The measured concentrations of PER ranges from 26.7 to 1020 ng/mL. Further analysis found that potential co-medicated anti-seizure medication (ASMs) could significantly reduce the concentration and concentration/dose ratios (C/D) of PER (P < 0.001).
Conclusion: This is the first TDM study of PER in China. With 50μL plasma, the analyte was prepared by acetonitrile protein precipitation. Isocratic elution with 2 minutes for each sample was used in this method, which significantly superior to the published studies using liquid-liquid extraction and gradient elution. This method has been successfully applied in clinical practice by TDM of PER in plasma samples of Chinese pediatric subjects. By this method, we firstly identified that the potential drug-drug interactions between PER and several concomitant ASMs were existed in

Chinese children, which were also in line with previous studies in patients of other race. These findings provide valuable information to enable clinicians for the reasonable application of PER in the future.

关键字 Perampanel; LC-MS/MS; Epilepsy; TDM; Drug interaction

分类：6. Clinical Pharmacology 临床药理
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Effects of growth hormone combined with gonadotropin-releasing hormone agonist (GnRHa) can improve the height of girls with central precocious puberty

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Background: Central precocious puberty (CPP) is triggered by the early activation of the hypothalamic-pituitary-gonadal (HPG) axis, resulting in inappropriate release of gonadotropin-releasing hormone (GnRH) and the onset of puberty. After years of clinical practice, GnRHa has become the standard treatment for CPP. However, some studies have shown that children with CPP can experience growth deceleration after GnRHa treatment, and ultimately fail to reach the ideal height. Therefore, GnRHa combined with rhGH may be a better choice for the treatment of CPP.
Objective: This study aimed to investigate the outcomes of gonadotropin-releasing hormone agonist (GnRHa) therapy with or without growth hormone (GH) therapy for girls with idiopathic central precocious puberty (CPP).
Methods: We conducted a retrospective analysis of CPP girls who attended the Pediatric Endocrinology Clinic of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology from January 1, 2017 to June 1, 2021. A total of 80 children with CPP girls aged 6-10 years old were treated for 30 months and were divided into the GnRHa group (group A, n=34), and the combined GnRHa/GH group (group B, n=46). All children were followed up every 3 months after treatment. They received regular tests including height, weight, and sex hormone levels, and pelvic B-ultrasound and bone age were measured every six months. The changes in height, weight, BMI, sex hormone levels and bone age were compared between the two groups.
Results: The initial CA was 8.0±0.8 years in group A, and 8.7±0.9 years in group B ($P<0.001$). There was no difference in height, weight, BMI, basic LH and FSH between the two groups before treatment, but the bone age had Statistical difference (9.2±1.1yrs vs. 10.3±1.0yrs, $P<0.001$). After treatment, it was found that the height improvement of group B was significantly higher than that of group A at 9th, 12th, 18th, 24th, and 30th months ($P< 0.001$). There was no statistical difference in body weight at each time point ($P>0.05$).
BMI was higher in group A than group B at each time point 12 months ago, which was statistically significant ($P<0.05$). However, there was no statistical difference at the 18th, 24th, and 30th months. There was no statistical difference between LH and FSH at each time point after treatment ($P>0.05$). There was a significant statistical difference between the two groups in terms of bone age before treatment (9.2±1.1 yrs vs 10.3±1.0 yrs, $P<0.001$, $t= 3.815$), there was no statistical difference at each time point after treatment ($P>0.05$).
Conclusion: Growth hormone combined with gonadotropin-releasing hormone agonist (GnRHa) can have more additional height gain than the GnRHa-alone group. And long-term treatment does not increase body weight, BMI and bone age progression.

关键字 Central precocious puberty ;Growth hormone;Gonadotropin-releasing hormone agonist

分类：6. Clinical Pharmacology 临床药理
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Predictive Performance of Pharmacokinetic Model-based Virtual Trials of Vancomycin in Neonates: Mathematics Matches Clinical Observation

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Abstract
Background: Vancomycin is frequently used for the treatment of Gram-positive bacterial infections in neonates. However there is still no consensus on the optimal dosing regimen. The aim of the current study is to assess the predictive performance of pharmacokinetic model-based virtual trials in predicting dose-exposure of vancomycin in neonates.
Methods: PubMed was searched for relevant vancomycin clinical trials in neonates in which the percentage of target concentrations achievements was reported. Monte Carlo simulations were performed using NONMEM software to predict dose-exposure, and the differences of outcomes between virtual trials and clinical observations were calculated.
Results: A total of 11 studies were identified from the literature. Fourteen dosing groups were included to evaluate the dose-exposure relationships. For the 10 dosing groups where the exposure indicator was trough concentration, the mean (SD) deviation between original studies and virtual trials in terms of target concentrations achievements were 3.0% (7.3%). Deviations between -10% and 10% accounted for 80% of dosing groups. For the other 4 dosing groups where the exposure indicator was steady state concentration, all deviations were between -10% and 10%, and their mean (SD) was 2.9% (4.5%).
Conclusion: Pharmacokinetic model-based virtual trials of vancomycin in neonates have a good predictive performance of dose-exposure in neonates and might assist in the optimization of dosing regimens in neonatal practice to avoid trial and error.

关键字 vancomycin, neonate, virtual trial, dose-exposure, Monte Carlo simulation.

分类：6. Clinical Pharmacology 临床药理
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A rare side effect of busulfan in veno-occlusive disease resulted from a GSTA1*B*B homozygote in a Chinese child

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Background：Busulfan is primarily metabolized by glutathione-S-transferase A1 (GSTA1). The GSTA1*B haplotype diminishes GSTA1 activity by 10-30%, but is scarce in Asains. Veno-occlusive disease(VOD) is associated with the high exposure of busulfan.
Method：An 11-years-old boy received hematologic stem cell transplant (HSCT) due to refractory acute mixed lineage leukemia. Busulfan was administered during conditioning regimen by standard dose. We performed therapeutic drug monitoring (TDM) to monitor the concentration of busulfan and calculated the area under the concentration-time curve (AUC) by the trapezoidal rule. We conducted the GST genotypes tests using the remaining blood samples of TDM.
Results: The child developed VOD on the 25th day after transplantation. The AUC0-6h of busulfan was 2611.44μM•min (Upper limit is 1350 μM•min). The child was GSTA1*B*B homozygote, which takes up only 0.7% in the Chinese population. The patient died at last.
Conclusion: Taking into account the genetic polymorphisms of GSTA1 may be used as a biomarker for VOD to decrease the risk of side effect of busulfan.

关键字 Busulfan; VOD; HSCT; GST genotype

分类：6. Clinical Pharmacology 临床药理
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Pharmacokinetics of Meropenem in an End-Stage Renal Disease Child Undergoing Continuous Venous－Venous Hemofiltration

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Background：Meropenem clearance is greater in children with acute kidney injury (AKI) who received renal replacement therapy (CRRT). However, no studies have shown how the clearance of meropenem would change in children with end-stage renal disease (ESRD) who perform continuous venous－venous hemofiltration (CVVH), a mode of CRRT.

Method：We reported a case of a child ESRD who received CVVH. We used the HPLC to determine the concentrations of meropenem before and during the process of CVVH. Afterthat, we obtained the pharmacokinetic parameters of meropenem with and withtout the influence by NONMEM and WinNonlin, respectively.

Results：We found that the clearance of meropenem doubled during CVVH in children with ESRD.

Conclusion：Additional dose of meropenem after CVVH is appropriate for children undergoing CVVH to ensure efficacy

关键字 Meropenem; End-Stage Renal Disease; Children; continuous veno-venous hemofiltration

分类：6. Clinical Pharmacology 临床药理
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Clinical utiliy of a model-based piperacillin dose in neonates with early-onset sepsis

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Aims: Early-onset sepsis (EOS) is a common disease in neonates with a high morbidity and mortality rate. Piperacillin/tazobactam has been used extensively and empirically for EOS treatment without clinically validated dosing regimens, although the population pharmacokinetics (PPK) of piperacillin in neonates has been reported. Therefore, we wanted to study the effectiveness and tolerance of a PPK model-based dosing regimen of piperacillin/tazobactam in EOS patients.
Methods: A prospective, single-center, phase II clinical study of piperacillin/tazobactam in neonates with EOS was conducted. The dosing regimen (90 mg·kg-1, q8h) was determined based on a previous piperacillin PPK model in young infants (Cohen-Wolkowiez et al., 2014) using NONMEM v7.4. The pharmacodynamics (PD) target (70%fT>MIC, free drug concentration above MIC during 70% of the dosing interval) attainment was calculated using NONMEM combined with an opportunistic sampling design. The clinical treatment data were collected.
Results: A total of 52 neonates were screened and 49 neonates completed their piperacillin/tazobactam treatment course and were included in this analysis. The median (range) values of postmenstrual age were 33.57 (range 26.14 - 41.29) weeks. Forty-seven (96%) neonates reached their PD target. Eight (16%) neonates experienced treatment failure clinically. The mean (SD, range) duration of treatment and length of hospitalization were 100.1 (62.2, 36.2 - 305.8) hours and 31 (30, 5 - 123) days. There were no obvious adverse events and no infection-related deaths occurred in the first month of life.
Conclusions: A model-based dosing regimen of piperacillin/tazobactam optimized was evaluated clinically and was tolerated well and effective for EOS treatment.

关键字 piperacillin, neonates, early-onset sepsis, dosing optimization, clinical validation

分类：6. Clinical Pharmacology 临床药理
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MicroRNA-221-3p 通过抑制 HIF-1α 激活改善丙戊酸耐药癫痫患儿的小胶质细胞活化和癫痫发作

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One-third of patients with epilepsy suffer from drug-resistant epilepsy (DRE). Valproic acid (VPA) is a classic anticonvulsant drug, and its resistance is a crucial predictor of DRE, but the exact pathogenesis is still unclear. Most patients with VPA-resistant epilepsy appear distinct inflammatory response and local hypoxia. Hypoxia-inducible factor (HIF)-1α is an essential effector molecule of hypoxia and inflammation, and exert therefore a significant effect on the development of VPA-resistant epilepsy. We sought to determine the effect of HIF-1α on children and mice with VPA-resistant epilepsy, and investigated the micro (mi) RNAs that regulate its expression. We established models of VPA-sensitive epilepsy and VPA-resistant epilepsy in mice, and demonstrated that they had significant differences in epileptic behavior and electroencephalography data. Through proteomics analysis, we identified that HIF-1α was overexpressed in mice with VPA-resistant epilepsy, and that it regulated expression of interleukin-1β and tumor necrosis factor-α. These results were confirmed by western blotting and ELISA. Increased expression of HIF-1α led to an increased number of microglia and induced their polarization from the M2 phenotype to M1 phenotype, which triggered the release of proinflammatory mediators. Data mining demonstrated that miR-221-3p expression was reduced in VPA-resistant epilepsy, and negatively regulated HIF-1α expression. Intervention using miR-221-3p mimics reduced HIF-1α expression markedly and suppressed microglia activation to produce proinflammatory mediators, which ameliorated epileptic seizures. These observations identified miR-221-3p/HIF-1α as a promising therapeutic and drug-development target for VPA-resistant epilepsy.

关键字 Valproic acid-resistant epilepsy, MicroRNA-221-3p, HIF-1α, Microglia, Neuroinflammation

分类：6. Clinical Pharmacology 临床药理
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Prognosis of values of MiR-495-3p/NCAPG on Children with High-risk Neuroblastoma Biomarkers for High-risk Neuroblastoma

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Objective: High-risk neuroblastoma, as a malignant tumor in children, accounts for approximately 15% of childhood cancer-related mortality. Methods: This study explored potential genes related to the prognosis of children with high-risk neuroblastoma through bioinformatics analysis, cell experiments, and verification of human samples. Download the gene expression profile of neuroblastoma from the GEO database, and analyze the differentially expressed genes that are significantly related to high-risk neuroblastoma. Results: Univariate COX and LASSO regression analysis determined that six genes (NCAPG, UBE2C, MELK, CCNA2, KIF15, and BIRC5) are associated with the prognosis of high-risk neuroblastoma. Among them, NCAPG has not been studied as a key gene. Follow-up biological function research. The results showed that knocking down NCAPG can inhibit the migration and invasion of neuroblastoma cells, increase the rate of cell apoptosis and reduce the level of Bcl-2. At the same time, the luciferase reporter gene analysis method shows that miR-495-3p can negatively regulate the expression of NCAPG. Q-PCR experiments show that miR-495-3p is down-regulated in children with high-risk neuroblastoma. Conclusion: It is inferred that miR-495-3p/NCAPG can be used as a prognostic biomarker for children with high-risk neuroblastoma to guide clinical treatment.

关键字 High-risk neuroblastoma; children; MiR-495-3p; NCAPG

Category: 6. Clinical Pharmacology 临床药理
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Population pharmacokinetics of rituximab in pediatric patients with frequent-relapsing or steroid-dependent nephrotic syndrome

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Abstract Content Rituximab is frequently used off-label for the treatment of frequent-relapsing nephrotic syndrome (FRNS) or steroid-dependent nephrotic syndrome (SDNS), but the relapse rate remained high and the dosing regimen varied widely. The objective of this study was to characterize rituximab pharmacokinetics (PK) in pediatric patients with FRNS/SDNS, and to investigate the differences in rituximab PK between patients with FRNS/SDNS and other disease populations.

Methods Fourteen pediatric patients received rituximab for FRNS/SDNS treatment were enrolled in a prospective, open-label, single-center PK study. A population PK model of rituximab was developed and validated, and PK parameters were derived for quantitative evaluation.

Results A two-compartment PK model best described the data. Body surface area was the most significant covariate for both central clearance (CL) and apparent central volume of distribution (V1). Patients with FRNS/SDNS exhibited a clinically relevant increase in rituximab CL compared to patient population with non-Hodgkin's lymphoma (NHL).

Conclusion This pilot study indicated that higher doses or more frequent regimens of rituximab may be required for optimal therapeutic effects in patients with FRNS/SDNS. Further clinical studies with more patients are warranted to confirm this result.

Key words rituximab; pharmacokinetics; children; nephrotic syndrome; dosing
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分类：6. Clinical Pharmacology 临床药理
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Effects of posaconazole and morbid state on tacrolimus population pharmacokinetics in Crohn disease children undergoing hematopoietic stem cell transplantation

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Background: The present study aimed to explore the effects of posaconazole and morbid state on tacrolimus population pharmacokinetics (PPK) in Crohn disease (CD) children undergoing hematopoietic stem cell transplantation (HSCT).
Methods: Tacrolimus concentrations, physiological and biochemical factors, and concomitant medications from 51 CD children undergoing HSCT were used to establish a PPK model using the nonlinear mixed effect (NONMEM), and steady-state concentrations of tacrolimus from children less than 20 kg at different doses were simulated by Monte Carlo method.
Results: Weight, concomitant medication of posaconazole were included as covariates. At the same weight, the relative values of tacrolimus clearances were 1: 0.43 in children without or with posaconazole. Compared to children without posaconazole, simulated tacrolimus steady-state concentrations at different doses for different body weights were all higher in children with posaconazole ($P < 0.01$). Additionally, the best probabilities of reaching the target were 0.6 mg/kg/day for children weighing 5-8.2 kg and 0.5 mg/kg/day for children weighing 8.2-20 kg, however, tacrolimus steady-state concentrations had large inter-individual variability in CD children undergoing HSCT.
Conclusions: Tacrolimus PPK was established in CD children undergoing HSCT for the first time, where posaconazole significantly increased tacrolimus concentrations, meanwhile morbid state of CD may also increase variability in tacrolimus concentrations by affecting the intestinal tract.

关键字 posaconazole, tacrolimus, population pharmacokinetics, Crohn disease, hematopoietic stem cell transplantation

分类：6. Clinical Pharmacology 临床药理
1204

The pharmaceutical care model and effect of the medication guidance for children in the respiratory department

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[Abstract] Objective: To explore the pharmaceutical care model of the medication guidance for children in the respiratory department by establishing a specific counseling room beside the outpatient pharmacy. Methods: 120 children who received inhalant use education under the guidance of medication in the respiratory department of our hospital from September to December 2020 were collected, and the medication guidance and evaluation of inhalants were carried out by pharmacists, then a second evaluation was conducted one month later, therefore, the effect of pharmacist intervention was examined. Results: After the pharmacist's guidance and correction, the number of incorrect operation steps of children decreased significantly. The frequency of making mistakes in using Symbicort Turbuhaler and Seretide for each patient decreased from 3.44 to 0.78, and from 3.11 to 0.71, respectively. Conclusion: This study integrates a variety of forms and approaches to help children correctly master the use of inhalation devices. Providing pharmaceutical care by establishing a specific counseling room beside the outpatient pharmacy can be effective for those who are in need for learning and training, resulting in improving compliance of inhaler usage and better disease control, and reducing the occurrence of adverse drug reactions. It is a beneficial attempt to actively and continuously provide pharmaceutical care.
[Key words] outpatient pharmacists; inhalant; pharmaceutical care

关键字 outpatient pharmacists; inhalant; pharmaceutical care

Category: 6. Clinical Pharmacology 临床药理
1270

Population Pharmacokinetics and Dosing Optimization of Melocillin in infants

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Abstract Content Mezlocillin, a semi-synthetic acylureido penicillin, is a broad-spectrum antibiotic widely used to treat bacterial infections in neonates. However, due to the lack of developmental population pharmacokinetic (PopPK) studies in neonates, there are a wide variation in dosing regimens in clinical practice. Therefore the purpose of this study was to describe the pharmacokinetic characteristics of meloxicillin in neonates, evaluate the factors influencing interpatient variability and suggest an optimal dosage regimen based on the PopPK model of mezlocillin.

Methods This was a prospective, single-center, open-label study. Blood samples were collected by using an opportunistic sampling method. Meloxicillin blood concentrations were determined by high performance liquid chromatography with metronidazole as internal standard. Clinical data of enrolled neonates who received intravenous meloxicillin were collected. A PopPK model of meloxicillin in neonates was established by using nonlinear mixed effect model (NONMEM) software. The effects of various covariables on pharmacokinetic parameters were estimated. The model validation was based on goodness-of-fit plots and bootstrapping, normalized prediction distribution errors. Monte Carlo simulation was performed for dose optimization. Therapeutic target was defined as the free drug concentration higher than the minimum inhibitory concentration (MIC) within 70% of the dosing interval.

Results A two-compartment model with first-order elimination was used to describe the PopPK of mezlocillin. Covariate analysis showed that postmenstrual age, serum creatinine concentration and current weight were significant covariates. Monte Carlo simulation demonstrated that for infections caused by E. coli, the currently used dosage regimen (50mg/kg q12h) resulted in 89.2% neonates achieving the therapeutic target, using MIC breakpoint of 4 mg/L. For infections caused by other bacteria, such as β-lactamase Staphylococcus aureus (MIC=32mg/L), only 32.3% of infants could reach target treated with maximum dose (100 mg/kg q8h). Therefore, it was suggested to switch to other antibiotics for infections caused by β-lactamase Staphylococcus aureus.

Conclusion The PopPK model of mezlocillin in neonates was established in this study that was stable and reliable, and the optimal dosage regimen based on the developmental PopPK model was recommendeded for neonatal infections.

Key words mezlocillin, population pharmacokinetics, infants, dosing optimization

Reference

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分类：6. Clinical Pharmacology 临床药理
1649

Analysis of clinical data of imipenem cilastatin in the treatment of 120 children with severe pneumonia

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Objective：Through the analysis of the data of imipenem cilastatin in the treatment of 120
children with severe pneumonia, in order to explore the clinical characteristics of imipenem cilastatin in the treatment of severe pneumonia, and to better guide the clinical treatment of children with severe pneumonia. so as to effectively reduce the mortality of severe pneumonia in children.Methods： We were collected
the general data , clinical data , laboratory dataimaging data and prognosis were analyzed
retrospectively.Results:There were 70 males and 50 females in the imipenem group, with a minimum ageof 0.08 years, a maximum of 13.9 years and a median age of 5.91 years. In the
non-imipenem group, there were 75 males and 45 females, with a minimum age of 0.25 years, a maximum of 13.83 years and a median age of 9.17 years. Compared with the non-imipenem group, the imipenem group had younger age (0.000), longer course of disease (P=0.000), more premature infants (P=0.034) and more assisted ventilation (P=0.003), longer ventilation time (P=0.002), and more patients with underlying diseases [congenital heart disease (P=0.000), low immune function (P=0.000) and energy protein malnutrition (P=0.001). In laboratory examination, compared with non-imipenem group, the levels of procalcitonin, glutamic pyruvic transaminase, glutamic oxaloacetic transaminase, hypersensitive troponin, brain natriuretic peptide precursor, creatine kinase isoenzyme, prothrombin time and activated partial thromboplastin time in imipenem group were higher than those in non-imipenem group (P<0.05). Hemoglobin and fibrinogen were lower than those in non-imipenem group (P<0.05). Multiple Logistic regression analysis showed that gram-negative bacteria infection (OR=19.187, 95%CI: 1.135-324.308), procalcitonin (elevated) (OR=1.957,95%CI: 1.244-3.079), glutamic pyruvic transaminase (elevated) (OR=0.974,95%CI: 0.956-0.992), prothrombin time (elevated) (OR=25.159, 95% CI:3.689-171.566) is an independent risk factor for the use of imipenem cilastatin in children with severe pneumonia. In the pathogen examination, the most common pathogen in imipenem group was gram-negative bacteria (P=0.000), followed by Escherichia coli (25 strains, 29.8%) and Klebsiella pneumoniae (18 strains, 21.4%). The most common virus was cytomegalovirus (13 cases, 52.0%). A total of 31 strains producing extended-spectrum β-lactamases (ESBLs) (17 Escherichia coli, 14 Klebsiella pneumoniae) and 7 multi-drug resistant strains (Acinetobacter baumannii) were detected. The drug sensitivity results showed that the resistance rate of Escherichia coli to ampicillin, cefotaxime and cefepime was close to 100%, and the sensitive rate to carbapenem antibiotics was more than 75%. The resistance rate of Klebsiella pneumoniae to ampicillin, cefotaxime, ceftriaxone and cefepime was more than 75%, and the sensitive rate to carbapenem antibiotics was close to 100%. The number of children with pulmonary consolidation in imipenem group was higher than that in non-imipenem group (P < 0.05). The hospitalization time of the imipenem group was longer than that of the non-imipenem group (P =0.000), and the number of cured children was less (P =0.000).

Conclusions：1. Severe pneumonia is more common in infants and young children. Imipenem
cilastatin is mostly used in children with severe pneumonia under 1 year old. 2. Children with severe pneumonia complicated with basic diseases such as preterm delivery, CHD, low immune function and protein and energy malnutrition are often treated with imipenem cilastatin. 3. Most of the children with severe pneumonia treated with imipenem cilastatin are complicated with liver function damage, abnormal blood coagulation, gram-negative bacteria infection, progressive elevation of PCT or pulmonary consolidation. 4. Imipenem cilastatin is highly sensitive to gram-negative bacteria producing ESBLs. 5. Children with severe pneumonia with long course of disease and long hospital stay may lead to low effective rate of treatment.

关键字 Children; Severe pneumonia; Imipenem; Cilastatin; Treatment; Drug resistance

分类：6. Clinical Pharmacology 临床药理
1652

Distribution of culturable specific anaerobes and drug resistance of Bacteroides anaerobes in fecal samples of hospitalized children in pediatrics

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Objective To analyze the distribution of culturable specific anaerobes and the drug resistance characteristics of Bacteroides anaerobes in fecal samples of pediatric hospitalized children in Hohhot, so as to provide experimental basis for guiding and standardizing the rational use of antibiotics in pediatric patients.Methods 272 fecal specimes were collected from February 2021 to June 2021 in the hospitalized children of the Affiliated Hospital of Inner Mongolia Medical University. Culture and identification of anaerobic bacteria, testing the antimicrobial sensitivity of Bacteroides by broth microdilution method, and collecting its clinical data. Results There were 136 specimens found anaerobic bacteria in 272 ,and the detection rate was 50.00%. (136/272) . 166 strains of obligate anaerobe were isolated and identified in our hospitai.There were 108 strains of gram-negative (65.06%) and 58 strains of gram-positive strains (34.93%). Bacteroidetes were dominant in gram-negative bacteria [91 strains(54.82%)] ,The gram-positive bacteria were mainly bifidobacteria [44 strains(26.51%)].There were 73 specimens found bacteroidetes in 272 ,and the detection rate was 26.84%. (73/272) .The detection rate of Bacteroides in stool samples of non-diarrhea group (29.52%) was higher than that of diarrhea group (17.74%),and the difference was statistically significant. The detection rate of Bacteroides in feces samples of 10 years old group was higher than that of 0~1 years old, 1~3 years old, 3~7 years old group, and the difference was statistically significant.Drug sensitivity results showed that the resistance rates of Bacteroides toclindamycin, ticarcillinan and clavulanic acid, piperacillin and triazolobactam and chloramphenicol were 96.70%, 5.49%, 3.30% and 2.20% .Besides,it to metronidazole and imipenem were 12.09% and 4.40%, respectively. Conclusions The obligate anaerobic bacteria isolated from fecal specimens of hospitalized children in pediatrics are mainly Bacteroides, which are resistant to a variety of antibiotics, including metronidazole and imipenem. .It should attract high attention. The isolation rate of anaerobic bacteria in fecal samples of children was related to diarrhea and the age of children.

关键字 Anaerobic bacteria; Bacteroides fragilis; Drug resistance

分类：6. Clinical Pharmacology 临床药理
1715

Photosensitivity induced by voriconazole in children with ABCB1 rs1045642 T/T genotype

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Objective: Voriconazole was the second frequently reported drug associated with photosensitivity. Few Chinese cases have been reported. Here we described a case of photosensitivity induced by voriconazole, who carried ABCB1 s1045642 T/T genotype.
Methods: The clinical data of a child with ABCB1 rs1045642 T/T genotype and skin photosensitivity induced by voriconazole in Beijing Children's Hospital were analyzed retrospectively. The clinical features were summarized and the literatures were reviewed by searching PubMed and Chinese national databases “WanFangData” and “CNKI”. The literatures about the relationship between ABCB1 gene polymorphism and voriconazole pharmacokinetics and adverse reactions were reviewed.
Results: A 6-year-old boy was diagnosed with primary immunodeficiency disease. Long-term oral voriconazole was administered for fungal infections prophylaxis and treatment. Skin light-distributed erythema and pigmentation occurred about 3-4 weeks after treatment. The skin lesions were significantly alleviated one month after the withdrawal of voriconazole. Pharmacogenomics of voriconazole showed ABCB1 gene rs1045642 T/T in the patient. Some studies have found that ABCB1 rs1045642 T/T genotype reduced the clearance rate of voriconazole, which might be possible reason for the erythema and pigmentation of the skin.
Conclusion: We reported a case of photosensitivity caused by voriconazole in a child, indicating the importance to monitor such adverse reaction of voriconazole in clinical practice. ABCB1 gene polymorphism is possible to correlate with the pharmacokinetics and adverse reactions of voriconazole. Further large-scale clinical studies are warranted to verify it, and thus facilitate personalized medication.

关键字 voriconazole; photosensitivity; ABCB1; pharmacokinetics; pharmacogenomics

Nursing

护理

Category: 19. Nursing 护理
77

A study on the status of information, motivation, behavior and influencing factors of pediatric nurses' prevention towards hospitalized children with medical device-related pressure injury

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Abstract Content Abstract　Objective　To explore the current status of pediatric nurses' prevention of medical device-related pressure injury in hospitalized children ,and to examine its influencing factors, so as to provide a basis for clinical teaching,training and building standardized prevention and control strategies.Methods　A cross-sectional survey was conducted among pediatric clinical nurses in six Grade-A hospitals in Guizhou Province using the self-compiled MDRPI Information-Motivation-Behavior Skills questionnaire and the influencing factors were analyzed.Results　A total of 504 valid questionnaires were completed from January to March 2020.The scores of the MDRPI Information-Motivation- Behavior Skill scale, knowledge information dimension, motivation dimension and behavior skill dimension were respectively (132.44±9.42), (22.63±4.28), (43.51±3.46) and (71.48±5.03).There were statistically significant differences in information dimensions among pediatric nurses of different ages, educational backgrounds and times of relevant knowledge training(P＜0.05).There were statistically significant differences in motivation dimensions among pediatric nurses of different ages, working years, professional titles and times of relevant knowledge training(P＜0.05).The differences in the dimensions of behavioral skills among pediatric nurses with different working years, professional titles and times of relevant knowledge training were statistically significant (P＜0.05).Multiple linear regression analysis showed that working years, professional titles, and the number of relevant knowledge training were the influencing factors for the total score of Information-Motivation-Behavior Skills in prevention of MDRPI.Conclusion　The motivation intention of pediatric nurses to prevent hospitalized children with MDRPI is positive, but the level of relevant information acquisition and behavioral skills need to be improved.Nursing managers should train the knowledge of prevention MDRPI according to the characteristics of different nurses, and establish positive cognition and behavioral improvement motivation intention through strengthening the knowledge,so as to guide the change of prevention practice ability and improve the nursing quality of hospitalized children.

Methods A cross-sectional survey was conducted among pediatric clinical nurses in six Grade-A hospitals in Guizhou Province using the self-compiled MDRPI Information-Motivation-Behavior Skills questionnaire and the influencing factors were analyzed.

Results A total of 504 valid questionnaires were completed from January to March 2020.The scores of the MDRPI Information-Motivation- Behavior Skill scale, knowledge information dimension, motivation dimension and behavior skill dimension were respectively (132.44±9.42), (22.63±4.28), (43.51±3.46) and (71.48±5.03).There were statistically significant differences in information dimensions among pediatric nurses of different ages, educational backgrounds and times of relevant knowledge training(P＜0.05).There were statistically significant differences in motivation dimensions among pediatric nurses of different ages, working years, professional titles and times of relevant knowledge training(P＜0.05).The differences in the

dimensions of behavioral skills among pediatric nurses with different working years, professional titles and times of relevant knowledge training were statistically significant (P＜0.05).Multiple linear regression analysis showed that working years, professional titles, and the number of relevant knowledge training were the influencing factors for the total score of Information-Motivation-Behavior Skills in prevention of MDRPI.
Conclusion The motivation intention of pediatric nurses to prevent hospitalized children with MDRPI is positive, but the level of relevant information acquisition and behavioral skills need to be improved.Nursing managers should train the knowledge of prevention MDRPI according to the characteristics of different nurses, and establish positive cognition and behavioral improvement motivation intention through strengthening the
knowledge,so as to guide the change of prevention practice ability and improve the nursing quality of hospitalized children.

Key words Pediatric;Medical Device-related Pressure Injury; Information-Motivation-Behavior Skills;Questionnaires;Nursing Administration Research
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分类：19. Nursing 护理
87

A study on the status of information, motivation, behavior and influencing factors of pediatric nurses' prevention towards hospitalized children with medical device-related pressure injury

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Objective To explore the current status of pediatric nurses' prevention of medical device-related pressure injury in hospitalized children ,and to examine its influencing factors, so as to provide a basis for clinical teaching,training and building standardized prevention and control strategies.Methods A cross-sectional survey was conducted among pediatric clinical nurses in six Grade-A hospitals in Guizhou Province using the self-compiled MDRPI Information-Motivation-Behavior Skills questionnaire and the influencing factors were analyzed.Results A total of 504 valid questionnaires were completed from January to March 2020.The scores of the MDRPI Information-Motivation- Behavior Skill scale, knowledge information dimension, motivation dimension and behavior skill dimension were respectively (132.44±9.42), (22.63±4.28), (43.51±3.46) and (71.48±5.03).There were statistically significant differences in information dimensions among pediatric nurses of different ages, educational backgrounds and times of relevant knowledge training(P＜0.05).There were statistically significant differences in motivation dimensions among pediatric nurses of different ages, working years, professional titles and times of relevant knowledge training(P＜0.05).The differences in the dimensions of behavioral skills among pediatric nurses with different working years, professional titles and times of relevant knowledge training were statistically significant (P＜0.05).Multiple linear regression analysis showed that working years, professional titles, and the number of relevant knowledge training were the influencing factors for the total score of Information-Motivation-Behavior Skills in prevention of MDRPI.Conclusion The motivation intention of pediatric nurses to prevent hospitalized children with MDRPI is positive, but the level of relevant information acquisition and behavioral skills need to be improved.Nursing managers should train the knowledge of prevention MDRPI according to the characteristics of different nurses, and establish positive cognition and behavioral improvement motivation intention through strengthening the knowledge,so as to guide the change of prevention practice ability and improve the nursing quality of hospitalized children.

关键字 Pediatric;Medical Device-related Pressure Injury; Information-Motivation-Behavior Skills;Questionnaires;Nursing Administration Research

分类：19. Nursing 护理
89

Value of peripheral perfusion index to predict acute limb ischemia in newborns after peripheral artery cannulation

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Background: Acute limb ischemia (ALI) is common complication of neonatal peripheral artery cannulation. It’s important to address as soon as the early signs of ALI. Peripheral Perfusion index (PPI) could aid in noninvasive evaluation of distal extremity perfusion in an effort to notify risk of potential ischemic injury from catheterizations.
Objectives: To investigate the feasibility of using PPI to monitor ALI in newborns after catheterizations.
Methods: A nested case-control study design was used. Clinical information of newborns who had been admitted to the Neonatal Intensive Care Unit of Jiangxi Provincial Children’s Hospital and had received peripheral artery cannulation from January 2018 to January 2020 was prospectively collected. Transcutaneous blood oxygen saturation (TcSO2), PPI, delta-PPI (ΔPPI1; the difference in PPI values of the two arms. ΔPPI2; difference in the PPI values before and after cannulation) were recorded.
Results: A total of 25 newborns with ALI were included in the study. These were then paired with 100 newborns without ALI. The PPI and TcSO2 of the cannulated limb were significantly lower in the ALI group than in the non-ALI (NALI) group ($P < 0.05$). The area under the receiver operating characteristic curve was significant for ΔPPI1. The ΔPPI1 had a sensitivity and specificity of 92% and 87%, respectively, for diagnosing ALI. ΔPPI1 greater than 0.315 suggested that the infant was at risk of ALI.
Conclusions: Monitoring the change in the PPI in newborns after catheterizations helped in the early assessment of ALI.

关键字 Keywords: Infant; artery cannulation; acute limb ischemia; peripheral perfusion index

分类：19. Nursing 护理
134

Experience of Homecare of Children on Automatic Peritoneal Dialysis During the COVID-19 Outbreak: A Qualitative Descriptive Study

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Background:
Disruptions of healthcare are ubiquitous with the COVID-19 spread and its attendant containment measurements. Peritoneal dialysis (PD) is a preferred dialysis modality for children with end-stage kidney diseases (ESKD) [1] and gains more popularity and attention in the COVID-19 era for its lower risks of acquiring COVID-19 compared with hemodialysis [2],[3]. However, caring for children on PD requires persistent efforts and may encounter many challenges, especially during the early stage of the COVID-19 outbreak with strong containment measurements[4]. Understanding the experience of caregivers with a child on PD during this special time will potentially facilitate the decision-making of dialysis modality and better support the home care of PD.
Objectives: To describe home care experience, challenges, coping strategies of caregivers with children on automatic peritoneal dialysis in mainland China during the early stage of the COVID-19 outbreak.
Methods: The qualitative descriptive approach is an important tool to study questions focusing on experience and perspectives[5]. We adopted this method because it aligns with the research aim of learning experience and gaining insights from families with children on PD. From February 2th to 10th, 2020, a purposive sample of 14 families with a child on automatic peritoneal dialysis from 11 provinces in mainland China was recruited with the maximum variation in COVID-19 caseload. The care routine, stress, and coping strategies of caregivers of children on peritoneal dialysis were collected using semi-structured telephone interviews. All interviews were recorded and transcribed verbatim and analyzed using thematic analysis. The study was reported according to the Consolidated Criteria for Reporting Qualitative Research (COREQ)[6]. To ensure the trustworthiness and credibility of the study[7], we adopted multiple approaches. The two researchers (RZ and QZ) who conducted the data collection and analysis had already established rapport and empathy with the participants before the interviews to gain depth of information. The severity of the coronavirus spread was considered with participants from various parts of China. The interview transcripts and the interpretation were sent back to caregivers for member-checking. RZ and QZ conducted initial coding of the data separately and then discussed and compared the codes and themes. Codes and themes were cross-checked within these two researchers (RZ and QZ) until the consensus was reached. Saturation was reached after twelve interviews, and we conducted another two to ensure saturation.
Findings: Four key themes were defined: (1) concerns of PD treatment intertwined with worries of COVID-19; (2) remaining a sense of normality in the middle of the challenges; (3) stay safe; (4) stay positive and carry on.
Conclusions: Families with children on automatic peritoneal dialysis addressed the stress from COVID-19 and its containment measures by closely adhering to COVID-19 preventative measures, actively adjusting the mentality, and managed to remain a sense of normality during the outbreak. Healthcare staff has played a key role in offering information and resources to sustain high-quality peritoneal dialysis

care. Institutional support should be ready to address the logistic and financial hardships to ensure the continuous care of children on peritoneal dialysis.

PS：I deleted part of the abstract due to the character limitations here. Full version of the abstract is attrached. Thank you.

关键字 COVID-19; Peritoneal dialysis; Pediatric; Caregivers; Experience; Coping; Nursing

分类：19. Nursing 护理
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Progress of early warning score research: a visual analysis based on Gephi and CiteSpace

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Objective: To explore the progress of early warning scores between 2010 and 2020 based on knowledge visualization analysis. Methods: The literature related to early warning score included in Web of Science(WOS) and China National Knowledge Infrastructure(CNKI) databases from 2010 to January 2021 were collected. The distribution of the published years, countries, research institutions, and authors were extracted and analyzed. Gephi 0.9.2 was used for generating a cooperative network to find the research power, regional distribution trends, and each cooperative relation. Meanwhile, CiteSpace 5.5 R2 was applied to analyze those high-frequency keywords and bursting keywords to build the map of co-citation reference, to explore the evolution of research in the field of early warning score, and the hotspots and frontiers about this field in recent 10 years. Results: A total of 870 Chinese journal articles and 1264 English journal articles on early warning score were collected, and the number of published literature increased steadily between 2010 and 2020. The impact factors of 34.3% of English literature were concentrated between 2 and 3, and 21.3% of literature were concentrated over 4. According to the knowledge visualization analysis, the United Kingdom published most of the related English articles in this field and shared the most cooperative connection with other countries, followed by the United States and Canada. In terms of research institutions, the number of papers issued by the University of Oxford ranked first (44). Meanwhile, there were 12 research teams involving 5 and more co-authors, among which the Smith GB research team from the University of Bournemouth ranked the first in the number of articles as well as the cooperation links with another research team. Besides, internal connection and cooperation between international institutions were frequent and sufficient. Through analyzing high-frequency keywords, the research hotspots mainly focused on the early warning scoring information system, early warning management mode, and validation of early warning scores for various specialized diseases such as multiple trauma and sepsis. By analyzing bursting keywords and co-citation reference, the research frontier mainly focused on Covid-19 triage, risk stratification of severe maternal and national early warning score, etc. Conclusion: there was a certain gap between China and leading countries in the field of early warning scoring research as more cooperation among research teams were required in China, and domestic research focuses on the early warning information system and early warning management mode of critical diseases were in great demand.

关键字 Keywords: Early warning score; Research hotspot; Research frontiers; Visualization analysis; CiteSpace; Gephi

分类：19. Nursing 护理
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Management of Follow-Up With Preterm Infants During the Outbreak in China

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Objective: To investigate the feasibility and effectiveness of a combination of online and face-to-face follow-up for preterm infants during the COVID-19 epidemic and to explore a follow-up pattern that can provide follow-up services while maximizing the protection of preterm infants and soothing the fear of their parents.
Methods: Preterm infants (n = 35) whose first follow-up appointment was scheduled from February 1 to April 30, 2020, and preterm infants (n = 43) in the NICU follow-up group who were discharged from January 1, 2018, to January 31, 2020, who had a second or later routine follow-up appointment scheduled from February 1 to April 30, 2020, were enrolled. We provided a combination of online and face-to-face follow-up for preterm infants surveyed with the Wenjuanxing platform before and after the online follow-up and compared the first-time follow-up rate between the outbreak and the same period of the previous year.
Results: Feeding and oral medicine and supplements were the most concerning problems of the parents of preterm infants. The anxiety level of the family was significantly decreased after online follow-up ($P < 0.05$). A total of 96.8% of parents were satisfied or very satisfied with online follow-up, and 95.2% of parents thought that online follow-up had answered all their questions. Only 35.5% of parents thought online follow-up could replace face-to-face follow-up.
Conclusion: The combination of online and face-to-face follow-up alleviated the anxiety of the parents during the outbreak and achieved a similar first-time follow-up rate as the same period in 2019.

关键字 follow-up, preterm infant, COVID-19, online, face-to-face

分类：19. Nursing 护理
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Effect and nursing experience of breastfeeding guidance for hospitalized newborns under COVID-19

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Objective: To explore the guiding effect and nursing experience of neonatal breastfeeding under COVID-19 Methods: between January 2020 to December 2020, selected in our hospital pediatric hospital and give new parents of 60 newborns breastfeeding as the research object, using the random number table method parents were randomly divided into two groups, group A for face-to-face education guidance, group B for video education guidance, and analyzed two groups of neonatal parents collect quality of breast milk Results: The difference in the quality of collected breast milk between parents of group A and group B was statistically significant ($P<0.05$).
Conclusion: Face-to-face breast-feeding guidance for parents of hospitalized newborns is helpful to improve the quality of breast-feeding and beneficial to the healthy development of infants, which is worth promoting in clinical practice.

关键字 novel coronavirus,newborn,breast feeding,health education

分类：19. Nursing 护理
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A Therapeutic Play Program Based on Stress and Coping Theory and Cognitive Development Theory for Children Undergoing Kidney Biopsy Procedure with Local Anesthesia: The Development and Feasibility Testing

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Abstract
Background
An ultrasound-guided percutaneous kidney biopsy is a safe procedure to understand pathological changes and establish the diagnosis, while it may cause anxiety and distress among children and their caregivers, especially for those children undergoing local anesthesia.
Aim
To develop a medical play program for children undergoing an ultrasound-guided percutaneous kidney biopsy with local anesthesia and to test the feasibility of the program.
Methods
A multidisciplinary team consisting of nurses, social workers, and nephrologists developed a medical play program using Lazarus & Folkman' transactional model of stress and coping and Piaget’s cognitive development and theory of play as a framework. We assessed the feasibility of the program by interviewing the four nephrologists conducting the kidney biopsy procedure and ten children-parent dyads.
Results
A prebiopsy medical play program led by nurses was developed. The main tools were a self-designed 15-page picture book named “ Renal Biopsy Treasure Hunt” and a set of biopsy package. The nurses will use these tools to help children understand the steps of the procedure and corresponding coping strategies. In-depth interviews with nephrologists, children, and their caregivers showed that the pre-biopsy medical play program is clinically feasible. The children and parents found it interesting, acceptable, and useful in helping children cope with the stressful biopsy procedure.
Conclusions
The pre-biopsy medical play program for children undergoing kidney biopsy with local anesthesia was feasible and well accepted by the nephrologists, children, and parents.

关键字 Therapeutic Play Program, children, Kidney biopsy, feasibility testing

分类：19. Nursing 护理
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Effects of exercise rehabilitation on pulmonary function, aerobic capacity and quality of life in children with bronchial asthma: a Meta-analysis

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Objective: To investigate the effects of exercise rehabilitation on lung function, aerobic capacity and quality of life in children with bronchial asthma. Methods: According to the PICOS principle, China National Knowledge Network (CNKI), CQVIP, Wanfang, SinoMed, Web of Science, Cochrane, PubMed, Embase, and CINAHL databases were used to search for all Chinese-English randomized controlled trials on the effects of exercise rehabilitation on children with bronchial asthma from 2000 to 2020. The Cochrane manual was used to systematically review the literature. Meta-analysis was performed using RevMan5.3. RESULTS: Sixteen articles were included, including 999 subjects. Meta-analysis results showed that compared with drug therapy, Drug therapy combined with exercise rehabilitation could improve the percentage of forced vital capacity (FVC%)[MD=2.75,95%CI(1.22,4.28),P<0.05] and the percentage of peak expiratory flow (PEF%)[MD= 6.16,95%CI(3.19,9.14),P < 0.00] in children with asthma, but the percentage of forced expiratory volume in the first second in the predicted value (FEV1%) [MD=0.55, 95%CI (-0.59,1.69), P= 0.34> 0.05] and the ratio of forced expiratory volume in the first second to forced vital capacity (FEV1/FVC%) [MD=0.06,95%CI(-0.15,0.27),P=0.59] were not significantly different between the two groups. Drug therapy combined with exercise rehabilitation could improve the VO2max of aerobic capacity in children with asthma [MD= 5.68,95%CI(4.02, 7.34),P < 0.00001]. Drug therapy combined with exercise rehabilitation could improve the quality of life [MD=0.49,95%CI (0.34,0.64), P<0.00001]. CONCLUSIONS: Drug therapy combined with exercise rehabilitation can improve pulmonary function (FVC%, PEF%), aerobic capacity and quality of life in children with asthma.

关键字 Exercise rehabilitation; Bronchial asthma; Children; Lung function; Aerobic capacity; quality of life; Meta analysis;

分类：19. Nursing 护理
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Scoping review of blood culturing volume for children

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Objective To summarize the current standard volume on blood culture collected for children, and clarify the relationship between blood volume and the bacterial detection rate or contamination rate. To provide support evidence for establishing chinese standard about blood culture volume for children. Methods A total of 1442 literatures were retrieved and 28 were included. Scoping review method was used to analyze the literatures from the aspects of study type, object, purpose, blood volume, sample size, evaluation index and result description. Results Most of the standards about blood volume taken in foreign hospitals were based on body weight, some were based on children's age, and some used fixed blood volume as standard. Conclusion The standards of blood volume collected for children vary greatly. The interpretations for the results are also inconsistent. Most of the literatures are observational studies and there is seldom data for Chinese children. Therefore, it is necessary to conduct a multi-center ,large-sample study to establish the standards of blood collection volume for Chinese children.

关键字 children; blood volume; scoping review; blood culture

分类：19. Nursing 护理
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Analysis on psychological resilience and its influencing factors among parents of children with brain tumor

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【Abstract】 Objective To probe into the psychological resilience and its influencing factors among parents of children with brain tumor. Methods A convenient sampling method was used to conduct a questionnaire survey on the parents of 200 children with brain tumor admitted to the neurosurgery department of Beijing children's hospital affiliated to capital medical university. Results There was a statistically statistically significant difference in the parents' psychological resilience score compared with the domestic norm (t =31.32, P≤0.01). The scores of depression, anxiety and stress of the parents of children with brain tumor were negatively correlated with their scores of psychological resilience. The score of social support was positively correlated with the score of psychological resilience. Age of the children with brain tumor and gender, age, residence, depression score and social support score of the parents of children with brain tumor were the main factors affecting the psychological resilience of the children's parents. Conclusion Focusing on the psychological state of the parents of children with brain tumor, and perform targeted and personalized psychological nursing intervention for children and their parents, so as to reduce the generation of negative emotions of the parents of children with brain tumor. At the same time, comprehensively evaluate the social support of children's parents, mobilize their effective social support forces, and guide them to adjust their mentality in time, so as to enhance the confidence of children and their parents to overcome the disease.

关键字 Brain tumor; Parents; Psychological resilience; Social Support; Depress; Anxiety

分类：19. Nursing 护理
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Practice of evidence-based nursing for children's peripheral venous blood specimen collection

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Objective To apply the best evidence of children's peripheral venous blood specimen collection to clinical practice, to form an evidence-based nursing practice standard for pediatric inpatient peripheral venous blood specimen collection, to improve the awareness rate of nurses evidence and the rate of clinical practice standards, and to increase the qualification of blood specimens It does not reduce the pass rate of venous blood sampling for one puncture. Methods From October 2020 to March 2021, based on the standard procedure of the continuous quality improvement model of evidence from the Fudan University Evidence-Based Nursing Center, the best evidence of peripheral venous blood specimen collection was applied to the clinic, and the obstacle factor analysis stage was combined with Ottawa The research application model analyzes the obstacles to the application of evidence and formulates feasible action plans. Before and after the application of the evidence, 26 nurses and 208 and 289 patients from the Department of Rheumatology and Immunology of a third-level children's hospital in Beijing were used as the research objects to carry out quality review and effect evaluation, and the on-site observation method was used to assess nurses compliance with the best evidence. Sexual indicators, using questionnaires to investigate nurses awareness of the best evidence, and the test center feedback on the pass rate of blood samples. Results The application of evidence can significantly improve the nurses awareness and compliance with the best evidence of peripheral venous blood sampling. The compliance of the 6 indicators with poor compliance before the application of evidence was significantly improved after the application of evidence (P＜0.01) , Including 5 indicators including patient identification, hand hygiene, tourniquet use, blood sample collection order, wearing disposable gloves, the other 1 indicator showed no significant improvement in double fixation (P>0.01); the nurses' awareness rate was low before the application of the evidence Five indicators were significantly improved after the application of evidence (P<0.01), including five indicators including the timing of children's fisting, two-person fixation and standing, the use of tourniquets, and the order of blood specimen collection; and the application of evidence can help improve The qualified rate of blood samples increased, and the difference was statistically significant (P<0.01); the application of evidence did not affect nurses operations, and the success rate of venous blood sampling once did not decrease (P>0.01). In addition, the evidence application process has formed an evidence-based practice standard for peripheral venous blood specimen collection outside the department at the system level, improved peripheral venous blood specimen collection equipment, and formed a peripheral venous blood specimen collection checklist, which was applied clinically and achieved good results. Conclusion Although the collection of peripheral venous blood samples is the most routine operation in the clinic, with the emergence of new evidence, it is still necessary to carry out evidence application items for this operation. The application of evidence can standardize the peripheral venous blood samples of nurses. The purpose of collecting standard operations is to increase the qualification rate of specimens and not increase the suffering of patients. Contribute to the improvement of clinical quality.

关键字 儿童；血标本；循证护理实践；质量改进

分类：19. Nursing 护理
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Analysis of Surgical Service of family members for children undergoing surgical treatment in tertiary hospitals Based on Kano Model

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Objective To investigate the needs of the families of hospitalized children with surgery based on the Kano model,and to provide basis for nursing services in the children's surgery department.**Methods** A total of 1445 family members of pediatric surgery patients in a tertiary hospital in Guangzhou area were selected and asked to fill out the needs assessment questionnaire by stratification and cluster sampling.The Kano model was used to classify the needs of family care services, and improvement strategies were proposed based on the analysis of the satisfaction-importance matrix diagram. **Results** Among the 23 items of children’s family needs, 11 were One-dimensional needs, 8 were Attractive needs, 1 was Must-be need, 3 were Indifferent needs, and no reverse needs.The matrix diagram analysis showed that there were 11 in the advantage area,1 in the expecting improvement area, 3 in the minor expecting improvement area, and 8 in the maintenance area. **Conclusion** Kano model can be used to obtain the needs of family members of hospitalized children with surgery and to improve nursing services at different levels.The Must-be need should be ensured.The One-dimensional Quality should be completed,and the Attractive Quality should be improved.Finally, the continuous improvement of the nursing quality of children with surgery will be realized.

关键字 Surgery;Family;Nursing care;Need;Kano Model

分类：19. Nursing 护理
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FOCUS-PDCA model promotes rationalization of preoperative antibiotic use time

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Objective To explore whether FOCUS-PDCA model reduces the unreasonable incidence of preoperative antibiotic use time. Methods The selected study subjects were children who were admitted to our department from Julyto December 2020 and used preoperative antibiotics as the intervention group(197 cases), and the children who used preoperative antibiotics from January to June 2021 as the control group(188 cases). The intervention group was managedby following the FOCUS-PDCA model, containing 9 steps involving Find, Organize, Clarify, Understand, Select, Plan, Do, Check and Act. The control group was managed by the conventional management method, namely monthly quality controlling, randomly supervising by the head nurse and the responsible group leader. The use time of antibiotics, the scores of nurses' relevant knowledge before and after the intervention, and the satisfaction of nurses, doctors, and anesthesiologists in the two groups of children were connted. The software SPSS 22.0 was used for data analysis, the count data was described by percentage, and the Chi-square test was used. The normal distribution of measurement data was described as the form of `x土s, and the skewed distribution was described as the form of M(SD), and independent sample t test or rank sum test was used, P value less than 0.05 means the difference was statistically significant. Results The difference in antibiotic use time between the two groups was statistically significant(P<0.05). The differences in the nurse factor, process factor and overall situation of unreasonable use of antibiotics between the two groups of children were statistically significant(P<0.05), and the incidence of the intervention group was lower than that of the control group; the nurses' knowledge scores before and after the intervention were compared, the difference was statistically significant (P<0.05), and the score after intervention was higher than before. Before and after the intervention, the group of nurses, doctors, and anesthesiologists had statistically significant differences in service quality satisfaction, feasibility satisfaction and overall satisfaction (P<0.05), and the scores after the intervention were higher than before the intervention, but they didn't have statistically significant differences in the work efficiency satisfaction (P>0.05). Conclusion The irregular use time of clinical antibiotics needs to be controlled. The study adopted the FOCUS-PDCA model to significantly improve the unreasonable use of antibiotics, improve the nurses' knowledge about antibiotic use before surgery, and improve the satisfaction of medical staff, providing reference for clinical nursing management. However, the limitation of this study was that it was a single-center, non-randomized controlled trial, and it was recommended to conduct further longitudinal and horizontal in-depth research in the future.

关键字 FOCUS-PDCA Mode; Preoperative; Antibiotic Use

分类：19. Nursing 护理
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Case management of one case of children with severe hand bruises caused by a treadmill

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Objective: To summarize the nursing experience of a child with severe hand abrasions caused by treadmills. Method: A case management team was formed. Assessment was made by case team members, including general condition assessment, pain assessment, wound assessment, etc. Upon admission, members of the case management team administered information about the child and provided a care plan, which showed a continuous process including the stage during admission, after admission, and after discharge, and adjust dynamically according to the actual situation. The nursing plan was carried out ,involving paying attention to pain care, optimizing wound care, implementing medication care, providing rehabilitation plans, attaching importance to psychological care, and following up after discharge. During the hospitalization, the patient experienced 10 major dressing changes. After discharge, scar repair and functional exercise were focused on. The following indicators were used to evaluate the treatment effect: the FLACC Pain Behavior Assessment Scale was used to evaluate the pain level of the child; the blood routine, rapid C-reactive protein, wound bacterial culture and other infection indicators were monitored; the Jebsen hand function test was used to evaluate the hand function, and the protractor was used to measure for the total range of motion of the finger joints, the Vancouver Scar Scale was used to evaluate the hypertrophic scar; the children’s family members were asked about their satisfaction. Results: After 20 days of meticulous hospitalization and specialist care and 18 months of long-term follow-up and continued care, this patient achieved satisfactory results. The pain score of the child decreased from 7 points on the first day after the injury to 0 points on the fourth day after the injury; on the seventh day after admission, the child had no fever, no nasal congestion and runny nose, no cough or sputum, and no redness, swelling, or oozing in the wound. All test indicators were normal; the wound was white when admitted, and the wound area was 5cm×10cm; on the 17th day after the injury, the wounds became rosy; the 21st day after the injury, the day before discharge, the child’s wound had no infection, the wound area was about 3cm×9cm; on the 32nd day after the injury, there was only a nail-sized residual wound, and the wound area was about 1cm×1.2cm; at the 8th week after the injury, the wound was well sealed. The hand function test time on admission was 9 minutes and 20 seconds, and the range of motion of each joint was rated as good. The 5th month post-injury hand function test time was 2 minutes 36 seconds, the back of the hand and middle finger were slightly hypertrophic, the scar score was 4 points, and the degree of motion of each joint was rated as excellent; the 18th month post-injury, hand function test time was At 2 minutes and 10 seconds, the scar hyperplasia on the wound surface is not obvious, the scar score was 1 point, and the degree of motion of each joint was rated as excellent. During the hospitalization, the family members of the patients were satisfied with the treatment and nursing; after discharge from the hospital, they were satisfied with the follow-up and treatment effect and prognosis. Conclusion: Combined with the case management model, a case of a child with severe hand abrasions caused by treadmills was implemented personalized nursing intervention. The child had no serious complications and had a good prognosis, which can provide reference for the treatment of treadmill wounds and the recovery of limb function.

关键字 Treadmill Abrasions; Children; Case Management

分类：19. Nursing 护理
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Effect of preoperative rehabilitation nursing plan on the psychological state of caregivers of children with developmental hip dysplasia

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Objective: To explore whether the preoperative rehabilitation care plan has an effect on the mental state of caregivers of children with developmental hip dysplasia. Methods: Convenience sampling was used to select 33 children with developmental hip dysplasia admitted to our department from January 2019 to December 2020. There were 7 boys and 26 girls, aged 13.58±11.93 months, hospitalization days were 5.70±4.90 days, 29 were unilateral, 4 were bilateral, 5 were pelvic osteotomy, and 12 were adductortomy. 16 cases of manual reduction and plaster fixation. After obtaining the informed consent of the children and their families, preoperative rehabilitation care plans were adopted to intervene, including preliminary preparation, psychological care, caregiver education, pre-rehabilitation training (muscle strength training, lung function exercise, etc.) and follow-up supervision. Using the Self-Rating Anxiety Scale (SAS) and the Chinese version of the Caregiver Preparedness Scale (CPS), the investigator investigated the children before the intervention, the day before the operation, and the first day after the operation. The caregivers were evaluated for anxiety and caregiver readiness, and the one-way question method was used before discharge to understand whether the caregivers were satisfied with the preoperative care plan, and perform the nursing service satisfaction evaluation. Data was collected and SPSS 22.0 statistical software was used for data calculation. Measurement data data was represented by (`x±s), repeated measurement data analysis of variance was used, count data was represented by (%). Two-sided test was used and $P<0.05$ indicated that the difference was statistically significant. Results: The results of SAS and CPS scores of the caregivers of the children were different at different time points, and the differences were statistically significant ($F=48.579$, $P=0.000$; $F=101.206$, $P=0.000$), and the scores of SAS on the day before the operation and the first day after the operation were lower than those before the intervention. The scores of CPS on the day before operation and the first day after the operation were higher than the scores before the intervention. The satisfactory with the preoperative rehabilitation care plan of caregivers of the children accounted for 84.85% and there were no unsatisfactory cases. Conclusion: caregivers of children with DDH with surgical treatment have certain psychological problems. By adopting the preoperative rehabilitation care plan, the anxiety state of caregivers of children with DDH was significantly relieved, care readiness was significantly improved, and the psychological needs of caregivers were catered to. However, due to the fact that there were not many cases of DDH with surgery treatment in our hospital in the past two years, the number of cases included in the study was small, and the research conclusions still lack a certain degree of authority. Therefore, it is still necessary to expand the sample size and carry out randomized controlled studies to further prove its role.

关键字 Preoperative; Nursing Plan; Developmental Hip Displasia; Caregivers; Psychological

分类：19. Nursing 护理
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Nursing care of a child with complicated ankle fracture and skin necrosis

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Objective: To summarize the nursing experience of a child with complicated ankle fracture associated with skin necrosis at the outer ankle. Methods: The patient, girl, 11-year-and-10-month years old was admitted to hospital for car accident trauma for more than 2 hours.The diagnosis was left ankle fracture (external ankle open fracture) + left distal ulnar and radius fracture + multiple systemic soft tissue contusion + closed chest and abdominal injury, accompanied with left ankle site open wound which was about 4cm length, had visible active bleeding, incomplete cutting edge and incision pollution.The pain management, anti-infection management, swelling management, wound management and so on was conducted, cooperating with fluid rehydration, nutritional support, functional exercise, psychological care, etc. Ulcer sticks were early used to ablate necrosis to reduce the pain; drugs changing was conducted frequently; necrotic tissue was observed; then alginate dressing was used to fill the skin damage, vacuum sealing drainage technology(VSD) after thoroughly debridement was adopted and the changes of vital signs and specialized conditions were closely observed. Results: After 40 days of careful care, the child discharged without nursing complications whose wound area was significantly reduced, and the wound healed well 3 weeks after discharge. Conclusion: The case of children with complex ankle fracture had good nursing effect, which can provide reference for clinical nursing practice.

关键字 Ankle Fracture; Skin Necrosis; VSD: Case Care

分类：19. Nursing 护理
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Investigation and analysis of nursing human resource allocation in PICU of children's general hospital

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[Objective] Based on the nursing activity score (NAS), to investigate the nursing workload and nursing human resource allocation,put forward reasonable suggestions, provide evidence for reasonable allocation and dynamic adjustment of PICU nursing human resource.
[Methods] This study is a descriptive study. Nursing activity score were used to investigate. From March 1st, 2019 to March 31th, 2019, the data were collected at three time points per day for 31 consecutive days. At the end of each shift, namely 16:00, 00:00 and 08:00, that is to evaluate the nursing workload and nursing human resource allocation of all shifts of all hospitalized children during this period.
[Results] A total of 2703 data on nursing workload and nursing human resource allocation were collected. The average score of NAS of children in PICU of children's general hospital was 58.63±10.81. As for the overall allocation of PICU nurses, the actual number of nurses in each shift of each patient is lower than the number of theoretical nurses should be allocated, the difference between the two is very significant ($P < 0.01$). The actual number of nurses per patient per shift in each shift was significantly lower than the number of nurses that should be allocated in theory ($P < 0.01$).
[Conclusion] The nursing workload of PICU in children's general hospital is the same as that of adult ICU or may be higher than that of adult ICU. The allocation of nursing human resources should also be equal to or higher than that of adult ICU. The overall allocation of nursing human resources and the allocation of each shift in PICU of children's general hospital are insufficient. The nurses are overloaded, especially the night shift nurses. Nursing managers should strive to improve the overall allocation of nursing human resources and the allocation of each shift. Nursing managers should allocate nursing human resources accurately according to the difference of nursing workload on different shift.

关键字 Intensive care unit; Nursing workload; Nursing activity score(NAS); Nursing human resources; Children

分类：19. Nursing 护理
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Summary of the best evidence for prevention of pressure injury in children

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Objective To search, evaluate and integrate the relevant evidence on the prevention of pressure injury in children, and summarize the best evidence, so as to provide operational reference advice and clinical practice guidelines for the prevention of pressure injury in children, so as to reduce the incidence of stress injury and improve the quality of care. Methods According to 6S model, Systematic retrieval of WOCN, NPIAP, EPUAP Website, Pan Pacific Stress Injury Alliance (PPPIA), International Stress Injury Guidelines (IPUG), New Zealand Wound Care Association website (NZWCS), Australian Wound Association (AW), CNKI, WanFang Data, BMJ British Medical Journal Best Practice, UpTo Date, Cochrane Library, Joanna Briggs Institute (JBI) Library, Medline, PubMed all the evidence on the prevention of pressure injury in children, including clinical practice guidelines, evidence summary, systematic review, randomized controlled trials, expert consensus, quasi-experimental studies, The retrieval period is from January 1, 2015 to June 1, 2021. The retrieved guidelines were independently evaluated by four guideline evaluators, and the quality of the other included literature was independently evaluated by two researchers who had received evidence-based system training. In addition, combined with the judgment of professionals, evidence was extracted and summarized for the literature that met the quality standards. Results A total of 49 literatures were included, including 2 BMJ best practices, 1 guideline and 11 systematic review. The best evidence included 40 pieces of evidence in 8 aspects, including risk assessment, skin assessment, nutritional support, device-related, therapeutic care, predisposition, surgical children and management strategies.
Conclusion This study summarizes the children's pressure best evidence of injury prevention, a line for clinical nursing staff to provide effective preventive measures and practice guidelines. Medical institutions should be established based on the point of evidence-based evidence into children's pressure injury prevention measures, establish standards and standard operating procedures and nursing measures to improve the patient's health outcomes and outcome.

关键字 Pressure injury; Children; pediatric; Severe children; Preventive measures; Evidence-based nursing; Clinical practice

分类：19. Nursing 护理
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Application and nursing of central venous catheter in children with hemophilia

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This paper reports the process and nursing of placing central venous catheter in children with hemophilia. First of all, hemophilia and intravenous therapy team work closely together, Pre-catheterization education for children and parents, Select the appropriate central venous catheter. The puncture and catheterization were performed by experienced and highly skilled intravenous therapy specialist nurses. Follow the doctor's advice to supplement coagulation factors on time to reduce the risk of bleeding. After catheterization, the puncture point should be observed closely, and the catheter should be used for guidance and continuous care. The patients were followed up for 11 months. The parents and the children received high acceptance of the catheter.

关键字 Hemophilia; Central venous catheter; PICC. Port; nursing

分类：19. Nursing 护理
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Research progress of Family-centered hospice care service model in pediatrics

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With the development of social civilization and the change of traditional moral concepts, the hospice care has become a social concern and is one of the key medical fields in China.Hospice care was explained in detail by the National Comprehensive Cancer Network (NCCN) in 2019. To be specific, hospice care is a holistic approach to health care that is centred on the patient and family, with an emphasis on improving painful symptoms. Meanwhile, palliative and supportive care is provided according to the needs, concepts and beliefs of patients and their families.According to the WORLD Health Organization (WHO), more than 250,000 children are diagnosed with cancer each year, and 90 percent of them die of cancer. Acquired Immune Deficiency Syndrome, congenital malformations and neurological diseases are common causes of death in children.To some extent, a child is the hope of a family. When a child is dying of an incurable disease, it is necessary to provide hospice care to ease the pain and allow the child to live out the final days in peace and comfort. Therefore, family-centered care (FCC) is in line with the health-centered care model under the new medical background and the core concept of hospice care.At present, the objects of hospice care are mainly elderly patients with chronic diseases and tumors. However，rare study is carried out on hospice care for children.. Hence, hospice care of children is also an important issue to be solved in building a healthy China.In recent years, China has paid more attention to hospice care and introduced various policies to advocate its development.In 2015, the State Council pointed out that the current health work is arduous, especially in the field of palliative care in the "Outline of The National Medical and Health Service System Planning (2015-2020)". In 2016, under the background of building a healthy China, the "Healthy China 2030" Plan outline issued by the Central Government. Meanwhile, this plan proposed that "we should pay attention to the whole course of life, from the fetus to the end of life";In 2017, China also issued three guidance documents related to hospice care, pointing out the direction for the development of hospice care in China, which will become a milestone in the development of hospice care in China.Article 36 of the Law for ‘the People's Republic of China on Basic Medical Care and Health Promotion’ promulgated on June 1, 2020 also includes hospice care and advocates the development of hospice care. This measure implements general Secretary Xi's important directive spirit of "striving to provide people with health and health services throughout the life cycle", which has laid a good foundation for the development of hospice care in China. Thus, the present situation and necessity of the development for children's hospice care are expounded in this paper. Then, the application effect of family participation in children's hospice care model on children's quality of life, family grief and doctor-patient relationship was summarized, and corresponding suggestions were put forward. This article aims to accelerate the standardization construction of the family participatory mode of hospice care in China, for further research, exploration is most suited to China's national conditions and with Chinese characteristics of localization family participatory mode of children's hospice

care and more suitable for children care patterns provide the basis of many forms of peace, and promote the development of children's hospice care in China.

关键字 Pediatrics; Hospice care; Family-centered; review

分类：19. Nursing 护理
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Health literacy status and influencing factors of parents with child occlusive bronchiolitis

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[Abstract] Objective To investigate the current situation of health literacy of parents of children with bronchiolitis obliterans (Bo) and analyze its influencing factors, to provide basis for all-round long-term management of children with Bo. Methods 108 children with Bo and their parents hospitalized in the respiratory department of a children's Hospital in Hunan Province from January to December 2020 were selected by convenient sampling method. General data questionnaire, health literacy scale for patients with chronic diseases and Family Resilience Scale were used to investigate. Results the total score of health literacy of parents of children with Bo was (101.71 ± 13.13), and the rate of health literacy was 66.7%; Univariate analysis showed that there were significant differences in children's age, parents' educational level, family monthly income, family location and family structure (P < 0.05); Pearson correlation analysis showed that family resilience was positively correlated with health literacy (P < 0.01); Multiple linear regression analysis showed that family monthly income, children's age and family tenacity score were the main influencing factors of Bo children's parents' health literacy (P < 0.05).Conclusion the health literacy of parents of children with Bo is at the medium level. It is suggested that medical staff formulate corresponding health education and intervention measures according to the influencing factors to improve the health literacy level of parents and promote the all-round long-term management of children with Bo.

关键字 Bronchiolitis obliterans; Children; Health literacy; Family tenacity

分类：19. Nursing 护理
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An Intervention Study on Improving Test Quality of Pulmonary Ventilation Function by Levitating Ball Breath Training in Children

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【Abstract】 Objective To explore the intervention effect of levitating ball breath training on quality improving of pulmonary ventilation function testing in hospitalized children. Methods The experimental epidemiology study was conducted, and 755 hospitalized children were selected as the research objects, of whom undergoing pulmonary function tests in respiration medicine department of a grade A children's hospital from May in 2020 to April in 2021. They were divided into experimental group and control group by random number table. Children in two groups were given routine exhalation instruction, and the children in experimental group were additionally given levitating ball breath training. Pulmonary ventilation function tests were performed on the second day and the last day of hospitalization, and the effect of exhalation training was judged by the quality control level on the second pulmonary function test. Results The proportions of the standard flow-volume curves during first pulmonary function test in control group and experimental group were 48.11% and 48.45%. Respectively, the main quality control problems were insufficient exhalation time and expiration platform. The children in experimental group could tolerate the exhalation training, 75.59% of whom insisted on the exhalation training every day and 79.00% of whom reached the training times standard per day. The main problem of the exhalation training was that the suspension time did not meet the standard. The control group was inferior to the experimental group in terms of the starting standard, ending standard, acceptance curve standard, and repeatability standard of pulmonary function testing when discharge ($P<0.05$), and the proportion of A-level reports (59.09%) was also lower than that of experimental group (67.45%) ($P<0.05$). Conclusion Levitation ball breath training can effectively improve the quality of children's pulmonary ventilation function detection, but the execution behavior and expiratory stability of breath training still need to be further strengthened.
[Keywords] levitating ball breath training, hospitalized children, quality of pulmonary ventilation function, intervention study

关键字 悬浮球呼气训练；住院儿童；肺通气功能检测质量；干预研究

分类：19. Nursing 护理
637

Investigation of time management situation of pediatric head nurses and correlation analysis

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[Abstract] **Objective** To explore the situation of time management of head nurses in pediatric wards and provide practical reference for nurse leaders to carry out time management more efficiently. **Methods** A current survey of time management was conducted among 41 head nurses in a Grade A children's Hospital for one week. The daily time usage of each head nurse was comprehensively acknowleged, and the corresponding management schemes and improvement measures were put forward. **Results** There were 41 head nurses attending this study including 1 male and 40 females, of which 12 with years of manage working less than 3 years, 15 with 3 ~ 10 years and 14 with more than 10 years. The mean percentages of time of all categories recorded by the head nurses are presented as follows in descending order: clinical practice work(168.48minutes), nursing quality control(146.89minutes), attending training(64.97 minutes), paperwork(38.02minutes), teaching or education work (35.37 minutes), coordination(28.35minutes)and information submission(6.42 minutes). The largest proportion of the younger head nurse's time was occupied by clinical practice every day (213.23 ± 63.76 minutes). On the contrary, the time spent in quality control management is less than that of senior head nurses (98.96 ± 65.21 minutes). The daily quality control time of head nurses with senior professional titles is more than that of head nurses with medium-grade professional titles, and the time of participating in front-line work was relatively short ($p < 0.05$)on the contrary. There was no significant statistical difference ($p>0.05$)between other issues such as communication, teaching and training, information reporting, etc. Of which the time spent by head nurses with different characteristics was similar. **Conclusion** The daily work of pediatric head nurses is complicated and detailed. They spend the longest time in clinical practice work, followed by quality control. The time distribution of head nurses with different characteristics is different. It is suggested that hospital should improve the pediatric head nurses' time management ability whose seniority and professional title are low through providing professional management ability or time management training program. At the same time, managers need to shorten the non management time and increase the time for head nurses to participate more quality management work by conducted multi-sector's cooperation, so the quality of pediatric nursing maybe improved continuously.

关键字 pediatric，head nurse，time management

分类：19. Nursing 护理
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Mediating effect of primary caregiver self-efficacy on self-care ability and medication compliance of children with refractory nephrotic syndrome

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【Abstract】
Objective To investigate the self-efficacy, self-care ability and medication compliance of primary caregivers of children with chronic refractory nephrotic syndrome (CDN), and analyze their correlation. To explore the mediating effect of primary caregiver self-efficacy on self-care ability and medication compliance of children.
Methods Forty-eight patients who visited the hospital from June 2020 to May 2021 were selected as subjects, and self-efficacy scale, self-care ability scale and medication compliance scale were used to investigate. The results were analyzed by correlation analysis and regression effect analysis.
Results he self-efficacy score of primary caregivers was (28.00±5.58), which was in the middle level. The total score of self-care ability (99.92±28.40) was in the middle level. The results of each item were similar. The compliance score was (5.35±1.03), which belonged to poor to moderate compliance. Self-efficacy was positively correlated with the total score of self-care ability (r=0.847, P<0.001). Self-efficacy was positively correlated with medication compliance (r=0.923, P<0.001). Self-care ability was positively correlated with the total score of medication compliance (r=0.903, P<0.001). The medication compliance of children with caregiver self-care ability was significantly predicted (P <0.001). Caregiver self-care ability had a significant predictive effect on self-efficacy (P <0.001). After introducing the variable self-efficacy, the predictive effect of caregivers' self-care ability on children's medication compliance was reduced (P =0.059). It suggests that there is a full mediation effect. The total effect value was 0.031, p<0.001 was statistically significant. The indirect effect value was 0.028, and the confidence interval was 0.021-0.037, excluding 0, which was statistically significant.
Conclusions The level of self-efficacy, self-care ability and medication compliance of primary caregivers was low to moderate. Self-efficacy had a full mediating effect between self-care ability and medication compliance.

关键字 Nephrotic syndrome; Self effect; Self-care ability; Medication compliance; Mediating effects

分类：19. Nursing 护理
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Best evidence Summary of for home oxygen therapy in children with bronchopulmonary dysplasia

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【Abstract】 Objective To retrieve and analyze the evidence of family oxygen therapy for children with bronchopulmonary dysplasia and summarize the best evidence. Methods According to the "6S" evidence model, a computer search was conducted on the American Guide Network, the Ontario Registered Nurses Association website, the British National Institute of Clinical Medicine Guide, the Scottish Intercollegiate Guide, the New Zealand Guide Group, the International Network Guide, and the WHO Guide Net, China Medical Pulse Guide, American Academy of Pediatrics website, Chinese Center for Evidence-Based Medicine website, UpToDate, clinical evidence database, best clinical practice database, Australia Joanna Briggs Institute Evidence-based Health Care Center database, Cochrane Evidence on home oxygen therapy for children with bronchopulmonary dysplasia in libraries, pubmed, web of science, CNKI, Wanfang database and other websites and databases. Including clinical decision-making, guidelines, evidence summary, expert consensus, etc. The search time limit is from the establishment of the database to September 2020. Two researchers independently evaluated the quality of the literature, and extracted and summarized the evidence that met the standards. Results Eight articles were finally included, including 1 clinical decisions, 3 guidelines, 1 evidence summary, and 2 expert consensus. The best evidence summarized includes 30. Conclusion This study summarized the best evidence for home oxygen therapy for children with bronchopulmonary dysplasia, and provided evidence-based evidence for medical staff.

关键字 Bronchopulmonary dysplasia; Home oxygen therapy; Evidence summary

分类：19. Nursing 护理
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Bibliometric Analysis of Research on Uncertainty in Illness in China from 2001 to 2021

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Objective: This study systematically analyzed the research status and problems of uncertainty in illness among patients in China, so as to provide a reference basis for related research in this field.
Methods: The database of China National Knowledge Infrastructure(CNKI), China Biology Medicine disc(CBMdisc), Chinese Medical Journal Database(CMJD), and Wanfang Database were used to search the relevant literature on uncertainty in illness published in domestic journals from 2001 to 2020, and the search results were analyzed by bibliometric methods.
Results: A total of 1023 articles were included and published in 256 journals, the overall number of publications has increased since 2005, but the number of publications has decreased in the last three years. The most studied literature was 244 (23.9%) in East China and 180 (17.6%) in Central China. Cross sectional survey was the most popular method of literature research, with a total of 552 articles (54.0%). The subjects were mainly adult patients, witj a total of 808 articles (79.0%). The main diseases studied were tumor diseases, with a total of 523 articles (51.1%). The research mainly focused on the related influencing factors, with a total of 555 articles (54.3%). The research literature supported by scientific research fund accounted for 22.1%.
Conclusions: The research on uncertainty in illness in China has attracted extensive attention, but the research methods and research contents still need to be improved. In the future, it is necessary to carry out large-sample, multicenter, high-quality randomized controlled research to better provide evidence-based basis clinical evidence and further explore intervention research.
Keywords: Uncertainty in illness; Literature analysis; Bibliometrics

关键字 Uncertainty in illness; Literature analysis; Bibliometrics

分类：19. Nursing 护理
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Application of node control theory in perioperative communication and operation efficiency management

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Abstract：Objective Explore the effect of node control theory in improving perioperative communication management, building an information communication system, and improving the efficiency of perioperative work. Methods Choose the time period from January 2019 to July 2020 for this study, of which January 2019 to September 2019 was the control group, and routine management was implemented, and September 2019 to July 2020 was the study group,management based on node control theory was implemented, 500 cases, 30 cases, and 30 cases of patients, surgeons, and nurses under the management of two groups were selected as a group. The connection time, preoperative preparation rate, medical staff and patient satisfaction were compared between the two groups. Results The time-consuming of sending the operation task to the ward to receive the task, sending the operation task to the transfer nurse to receive the task, transferring the nurse to receive the task to arrive at the ward, transferring the nurse to arrive at the ward to arrive at the operating room, children to arrive at the operating room to enter the operating room, and operating room to send the operation task to the children to enter the operating room of the study group were (3.09±0.43) min, (2.07±0.46) min, (1.49±0.27) min, (4.36±0.98))min, (2.15±0.64)min, (13.30±2.73)min,which were significantly shorter than the control group (5.52±0.68)min, (2.34±0.54)min, (1.81±0.33)min, (8.94±1.46)min , (2.66±0.75) min, (20.63±3.69) min, the difference were statistically significant (P<0.05); the study group had insufficient fasting time, imperfect case data, lack of preoperative markers, causes of the child, and surgery preparatory forgetting and replacement of indwelling needles accounted for 0.40%, 1.20%, 0.80%, 1.60%, 0.20%, and 0.60%, which were significantly lower than those of the control group of 2.40%, 9.20%, 3.60%, 10.40%, 1.40%, 2.60%, the preoperative preparation rate was 95.20%, which was significantly higher than 70.40% in the control group, and the difference were statistically significant (P<0.05); the satisfaction levels of surgeons, nurses, and patients in the study group were 96.67%, 93.33%, 96.60%,which were significantly higher than the 76.67%, 73.33%, 82.40% of the control group, the difference were statistically significant (P<0.05). Conclusions Node control theory in perioperative communication and surgical operation efficiency management can shorten the time it takes for the operating room to send the surgical task to the child entering the operating room, improve the preoperative preparation rate, at the same time, it can improve the satisfaction of patients, nurses, and surgeons with management, which is worthy of application and promotion.
Key words:communication; operational efficiency; node control theory; perioperative period; preoperative preparation rate; satisfaction

关键字 沟通；手术运行效率；节点控制理论；围术期；术前准备完备率；满意度

分类：19. Nursing 护理
762

Evaluation of nursing effect of rubber dam for endodontic treatment of deciduous teeth

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Objective To evaluate the effect of rubber dam on the success rate of root canal treatment and satisfaction of quality nursing, and to provide evidence for clinical nursing in the future.

Methods 200 children aged 3 to 12 years who needed endodontic treatment of deciduous teeth in our hospital from December 2020 were randomly divided into intervention group (100 cases) and control group (100 cases).The intervention group was treated with rubber dam and the control group with cotton ball and saliva suction.The success rate of endodontic treatment of deciduous teeth after treatment was compared, and the satisfaction evaluation of nursing was used to evaluate the satisfaction degree of parents of the two groups on the quality of nursing and it also reflects the comfort degree of oral treatment from children.

Results The total effective rate of the rubber barrier group was 92%, which was higher than that of the control group (80%). The nursing satisfaction of the rubber dam group was 90% and that of the control group (60%). The difference between the two groups was statistically significant ($P<0.05$).

Conclusion The rubber dam can improve the treatment effect of the root canal treatment of deciduous teeth, which can improve nursing care and the satisfaction of patients and their parents. The rubber dam should be popularized in clinical oral treatment in the future.

关键字 rubber dam; Child; endodontic treatment of deciduous teeth ;nursing

分类：19. Nursing 护理
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Comparison the effect of non-nutritive sucking and white noise applied to preterm infants' first procedural pain and physiological parameters in a neonatal intensive care unit: A randomized controlled trial

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Background: Pain from heel stick in preterm infants have short-and long-term adverse sequelae. Currently pain management includes non-nutritive sucking(NNS), oral breast milk, facilitated tucking, nesting positions, breast milk smell, kangaroo care, oral sucrose, auditory interventions and the combined two or more of them. But the white noise used in premature infants were limited in China and no study has compared the effects of NNS and white noise on preterm infants.
Objective: To compare the effects of NNS and white noise on PIPP-R scores, heart rate, oxygen saturation, the time of crying and painful face of premature infants in a neonatal intensive care unit (NICU).
Methods: This experimental, parallel, randomized controlled research was conducted in a state hospital tertiary-level NICU. A total of 94 infants were randomly allocated to the NNS group (n=30), the white noise group (n=32), combined NNS and white noise group (n=32). In three groups, heart rate, oxygen saturation, the time of crying and painful face were measured and pain score was evaluated by two observes using Preterm Infant Pain Profile-Revised (PIPP-R) pre, during, and 1 minute after blood sampling by heel stick.
Results: There was a statistically significant difference between the groups in favor of the combined group in terms of change in the PIPP-R values and oxygen saturation during heel stick ($p<0.05$). A significant increase in oxygen saturation during and low PIPP-R scores post heel stick were found in the white noise group and combined group ($p<0.05$). Significant declines in heart rate was only found between white noise group and NNS group pre heel stick ($p=0.001$). Non-significant were found in the time of crying and painful face among the three groups ($p>0.05$).
Conclusion: Combined white noise and NNS used alone is more useful for relieving pain and increasing oxygen saturation in preterm infants compared with NNS during and after heel stick procedure. But compared with white noise, the combined method may be more benefit to reduce pain only during heel stick procedure. Meanwhile, white noise is more useful for relieving pain and increasing oxygen saturation in preterm infants compared with NNS after heel stick procedure.

关键字 white noise； non-nutritive sucking； preterm infants；procedural pain

分类：19. Nursing 护理
778

Application of continuous nursing intervention based on mobile health technology in children after interventional cardiac catheterization for congenital heart disease

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Aim To study the application of continuous nursing intervention based on mobile health technology in children after interventional cardiac catheterization for congenital heart disease (CHD).**Methods** Two hundred and six pediatric patients with CHD who successfully underwent interventional therapy in our department were selected as the research objects. These patients were randomly divided into the control group (n=103) and experimental group (n=103). After discharge, the control group received routine follow-up nursing intervention, and the experimental group received continuous nursing intervention based on mobile health (M-health) technology. After one year of follow-up, the quality of life, compliance scores, and the rehospitalization rate of the two groups was analyzed.**Results** The total score of quality of life in the experimental group was 84.36±9.49, which was significantly higher than that in the control group (67.74±10.45) ($P < 0.05$). The indexes of taking medicine on time, regular re-examination, reasonable work time, and reasonable diet in the experimental group were significantly better than those in the control group ($P < 0.05$). 4.85% of patients (n=5) in the experimental group were hospitalized due to infection or cardiac insufficiency and 11.6% of patients (n=12) in the control group were hospitalized. The rehospitalization rates showed a significant difference between the two groups ($P < 0.05$).**Conclusion** The application of continuous nursing intervention based on M-health technology in patients with CHD after interventional surgery is effective. It can significantly improve the quality of life and compliance of the patient, and reduce the readmission rate. Therefore, it is worthy of clinical application.

关键字 先天性心脏病；移动医疗技术；延续性护理

分类：19. Nursing 护理
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Survey the Status of exclusivebreastfeeding and related influencing factors in children hospitalized from discharge to 6 months of age in Chongqing, China: A cross-sectional analysis

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Objective: investigated the current status of exclusive breastfeeding of hospitalized children in Chongqing from discharge to 6 months of age and analyzed the influencing factors.

Methods: The mothers of the children who were discharged from a third-class Children's Hospital in Chongqing from June 2019 to July 2020 were selected as the subjects, the mothers were investigated with General questionnaire, breast-feeding quality rating scale, breast-feeding knowledge questionnaire and telephone follow-up, logistic regression analysis was used to analyze the influencing factors of exclusive breastfeeding from discharge to 6 months.

Results: The questionnaire was completed by 555 mothers and the effective recovery rate was 80.3% . From discharge to 6 months of age, 234 cases (43.8%) were exclusively breastfed, 156 cases (29.2%) were mixed-fed, 144 cases (27%) were artificial-fed, 14.76 ± 3.193,124 cases (31.8%) were breast-fed. The total score of breast feeding knowledge was (11.82 ± 3.616) , which was above average. Mothers of discharged infants described the most common feeding problems as insufficient breastfeeding, lack of feeding skills, and stress at work affecting breastfeeding. Dual logistic regression showed that the expected feeding pattern, premature delivery and pre-hospital feeding pattern were the main factors influencing exclusive breastfeeding after discharge ($p < 0.05$).

Conclusion: The rate of exclusive breastfeeding of hospitalized children in Chongqing from discharge to 6 months of age is slightly higher than the rate of exclusive breastfeeding of 6-month-old infants in the country, which is related to the investigation of the hospital as a baby-friendly hospital, but has not yet reached the national standard of 50%. The behavior of exclusive breastfeeding is mainly affected by the feeding method that family members want, whether it is premature or not, and the feeding method before hospitalization. It is recommended that children should strengthen the education of the method of breastfeeding maintenance of the mother during the hospitalization, and pay attention to family members while interfering with the mother's behavior. Understanding of feeding methods, expanding the scope of health education, adopting strategies to promote the importance of strengthening exclusive breastfeeding for family members and the handling of common feeding problems and other breastfeeding-related knowledge to promote family members' tendency to choose exclusive breastfeeding, and greatly Most parturients start to resume work three months after giving birth. When the work pressure is too high, it may affect the mother's lactation and even cause the mother to give up breastfeeding. Therefore, it is necessary to call on the government to strengthen the supervision of social enterprise units to effectively protect breastfeeding women. At the same time, professional caregivers should provide mothers with relevant strategies to maintain exclusive breastfeeding during work and reduce their own stress, as needed, to help mothers achieve a good balance between work and breastfeeding. The society and the government should be at work. In order to provide

more feeding support to mothers in order to further increase the rate of exclusive breastfeeding of hospitalized children after discharge. The survey object of this study is only from a hospital, which serves as a national three-level A comprehensive children's hospital and a national children's regional medical center (Southwest), the National Center for Clinical Medicine, to a certain extent, can represent the exclusive breastfeeding of sick babies in Chongqing after they are discharged from the hospital, but retrospective research has its own limitations, to understand the exclusive breastfeeding of sick babies in Chongqing after they are discharged from the hospital And influencing factors still require further multi-center, prospective cohort studies

关键字 hospitalized children; exclusive breastfeeding rate; influencing factors

分类：19. Nursing 护理
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Wound pain management accelerates the recovery of children undergoing laparoscopic day surgery: A randomized controlled study

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Abstract:
Objective To explore the application effect of pain management based on the concept of Enhanced Recovery After Surgery (ERAS) combined with ropivacaine incisional infiltration in postoperative care of children with laparoscopic day surgery.
Methods 120 pediatric patients underwent laparoscopic day surgery were randomized into ERAS group, integrated management group and control group, 40 cases per group. The groups were managed with traditional protocol, ERAS protocol and ERAS protocol combined with ropivacaine incisional infiltration, respectively. Visual analog scale (VAS) scores were recorded at postoperative 30 min, 1 h, 3 h, 6 h, and 24 h, as well as the postoperative time to get out of bed, postoperative length of stay, the incidence rate of postoperative adverse reactions and complications, the use of pain relieving medicine, and nursing satisfaction.
Results The VAS scores at postoperative 30 min, 1 h, 3 h, 6 h, and 24 h of the patients in the ERAS group were lower than those in the traditional group, but higher than those in the integrated management group($P<0.05$); The postoperative time to get out of bed, postoperative length of stay, the incidence rate of postoperative adverse reactions and complications, the use rate of pain relieving medicine in the integrated management group and ERAS group were lower than that of the control group, while the nursing satisfaction was higher than that of the control group. The time of postoperative time to get out of bed in the integrated management group was shorter than that of the ERAS group, the use rate of pain relieving medicine was lower than that of the ERAS group, and the nursing satisfaction was higher than that of the ERAS group (all $P<0.05$).
Conclusion The application of pain management based on the ERAS theories combined with ropivacaine incisional infiltration during the daytime operation can relieve postoperative pain, reduce the incidence of postoperative adverse reactions and complications, accelerate the postoperative recovery and improve nursing satisfaction in pediatric patients undergoing laparoscopic abdominal surgeries.

Key words enhanced recovery after surgery; incisional infiltration; pain management; laparoscopic day surgery

关键字 enhanced recovery after surgery; incisional infiltration; pain management; laparoscopic day surgery

分类：19. Nursing 护理
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Stigma and its related factors in the parents of epileptic children

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Objective: To investigate the stigma and its related factors in the parents of epileptic children.

Methods: Totally 123 parents of epileptic children were included by successive sampling from ShenZhen Children's Hospital during August 2020 to January 2021. The general information questionnaire and parental stigma scale were used to collected data. The general data of the children and their parents were collected by questionnaire survey, which was designed by the researchers by referring to relevant literature, including the children part (9 items) and the parents part (26 items). The parental stigma scale was used to evaluate the parental stigma, and multiple linear regression analysis was conducted on the factors affecting the parental stigma of the children.

Results: The score of stigma in patients of epileptic children was 2.90±0.55.Research showed that the stigma of patients of epileptic children was related to，number of children’s common diseases(b=0.122,beta=0.169), number of comorbidity(b=0.107,beta=0.175) and psychological status of parents(b=0.231,beta=0.374).

Conclusion: The stigma level of parents of epileptic children in China is higher than that in developed countries. The longer the course of disease, the more common diseases and the more anxious parents were, the higher the stigma of parents of epileptic children.

关键字 epilepsy stigma

分类：19. Nursing 护理
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Study on the effect of high simulation scene scenario simulation teaching on standardized training of pediatrics nurses

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[Objective] To explore the influence of high simulation situational simulation teaching on critical thinking of nurses in standardized training by formulating and implementing high simulation situational simulation teaching.
[Method] A total of 111 nurses of grade 2019 who were trained received standardized training in our hospital from January to December 2020 were selected as the object of this study.
[Research methods]
The nursing department set up a team of scenario simulation tutors, selected 30 head nurses, educational nurses and specialist nurses, and conducted 46 class hours of high simulation simulator (LLEAP) software use, case design, case operation, guiding guided feedback theory and practical exercises.
Case design: referring to the complete real cases of clinical data, the themes of four situational simulation cases were determined, which were pneumonia complicated with respiratory failure, intravenous infusion complicated with anaphylactic shock, nursing evaluation of children with acute peritonitis and difficulty in gastric tube placement. The simulated plot design includes common clinical nursing situations, such as disease observation, nursing evaluation, basic and specialist care, doctor's order treatment, clinical critical thinking and humanistic. All cases go undergo a first draft-revision-trial run-re-revision-finalization process.
Case implementation: The nurse participants were divided into 16 groups with 7-8 persons in each group. The simulation instructors, simulation center staff, and the standardized participants prepare correspondingly according to different divisions of labor. Before class, all participants have completed the theories and skills training related to the case and passed the assessment. Implement one case every month, four times a week, two instructors are responsible for each time, and a total of sixty-four such same training were implemented in four months.
Evaluation: The Critical Thinking Tendency Scale was used to compare the participants' critical thinking before and after training. The assessment content includes 70 items in 7 dimensions, including finding the truth, open mind, analytical ability, systematic ability, self-confidence of critical thinking, desire for knowledge and cognitive maturity, using Likert 6-point system in the evaluation. If the individual score is higher than 40 points, it indicates that the characteristic is strong. The total score of more than 280 points indicates that the subject has positive critical thinking ability.
[Results] The differences in the 7 dimensions and total scores before and after the high-simulation scenario simulation teaching were statistically significant($p < 0.05$). The standardized training nurses have strong critical thinking after the scenario simulation training.
[Conclusion] The teaching model based on high simulation can effectively and rapidly improve the enthusiasm of standardized training of nurses.The teaching model requires nurses to actively participants, open their minds, find the truth, cultivate analytical skills, stimulate curiosity, and ultimately promote and improve critical

thinking skills, thereby improving job competence. Therefore, this teaching model is worth promoting.

关键字 高仿真情景模拟；儿科护士；规范化培训

分类：19. Nursing 护理
875

Prevalence of Medical Adhesive-Related Skin Injury and Effect of a Barrier Film in Preterm Infants

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Background: In healthcare, medical adhesives are widely used to affix components to the skin. If not used properly, adhesive products may cause medical adhesive-related skin injury (MARSI), a prevalent but under-recognised complication.
Aim: To ascertain the prevalence of MARSI in preterm infants and the effect of using a barrier film (BF) to prevent such injuries.
Design: A cohort study and a randomised controlled study.
Methods: The sample group comprised 276 preterm infants from a level III neonatal intensive care unit. During the cohort study period, we prospectively observed the incidence, type, site, and occurrence time of medical adhesive-related skin injury in 196 premature infants. During the randomised controlled study period, 80 preterm infants were randomly assigned to group C (control) and group BF. The indicators observed were the same as those observed during the first period, and the incidence of infection, hospital length of stay, and cost were recorded.
Results: The prevalence of MARSI was 19.4% overall, 63.6% at £28 weeks, 28.0% at 28–32 weeks, and 8.1% at >32 weeks gestation. Skin tear (55.3%) was the most common injury type, and the face (42.1%) was the most vulnerable site for MARSI. Overall, 84.2% of MARSI occurred within 2 weeks of admission. The incidence of MARSI was lower in group BF than in group C ($P<0.05$). There were no statistical differences in other indicators between the groups (all, $P>0.05$).
Conclusions: MARSI is common in preterm infants. The lower the gestational age, the higher the prevalence of MARSI. Application of a BF is safe and can reduce the prevalence of such injuries in preterm infants.
Relevance to Clinical Practice: MARSI may cause pain, increase the risk of infection, and delay healing. Evidence-based bundle care should be encouraged to reduce the risk of MARSI.

关键字 barrier, epidermal stripping, medical adhesive-related skin injury, preterm infants, skin tear

分类：19. Nursing 护理
922

Investigation on the Status of Postpartum Depression in Children with Enterostomy and Analysis of Influencing Factors

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Abstract: Objective To understand the current status of postpartum depression of children's mothers undergoing enterostomy during the neonatal period, and to explore its influencing factors. Methods From March 2021 to August 2021, the mothers of 47 children who underwent enterostomy in the neonatal period admitted to a third-level a children's hospital in Shenzhen were selected as the research objects. The general information questionnaire, the specialist information questionnaire and the Edinburgh Postpartum Depression Scale (EPDS) were used for questionnaire surveys. Chi-square test, Spearman rank correlation analysis and Logistic stepwise regression were used to analyze the influencing factors. Results Forty-seven children's mother who underwent enterostomy during the neonatal period had an EPDS postpartum depression scale score (14.21±7.068), 40 with a score of 10 accounted for 85.1%, and 7 with a score of 10 accounted for 14.9%. 76.6% of the change in the center, 76.6% of the fun change, 89.4% of the excessive self-blame, 91.5% of the anxiety for no reason, 89.4% of the fear of no reason, 87.2% of the insomnia, and the ability to cope. Those who fell accounted for 83%, those who felt sad accounted for 85.1%, those who cried because of unpleasantness accounted for 76.6%, and those who thought of self-harm accounted for 40.4%. The analysis showed that the average monthly income of the children's mothers and whether the children had an intestinal stoma and surrounding skin complications had a difference in the incidence of mothers' postpartum depression (P＜0.05); The different stages of the postoperative period and the occurrence of intestinal stoma and surrounding skin complications are related to the incidence of postpartum depression in the mother (P<0.05); regression analysis shows whether the child has medical insurance and whether the intestinal stoma and surrounding skin occurs Complications have statistical significance for the incidence of mothers' postpartum depression (P<0.05). Conclusion The incidence of postpartum depression in mothers who underwent enterostomy during the neonatal period (85.1%) was significantly higher than that of premature infants hospitalized in NICU (40%), and self-harming thoughts were more common (40.4%). The occurrence of postpartum depression in mothers of children with intestinal stoma is closely related to whether the children have medical insurance and whether the complications of the intestinal stoma and surrounding skin occur. It is necessary for clinical nursing to focus on the psychological state of the mother of the child and to carry out further intervention research.

关键字 Enterostomy; Children; Mother; Postpartum depression; Current status

分类：19. Nursing 护理
954

Postoperative monitoring of cardiac combined valve lesions

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Objective Dicuspid valve and aortic valve lesions are more common in cardiac combined valve disease, and aortic valves with tricuspid valve lesions are rare. Share refined and high-quality nursing after pediatric aortic valve tricuspid valve combined with valve lesions, increase the success rate after surgery and shorten the hospitalization time.
Methods A case of fine and high-quality nursing after secondary surgery of aortic valve tricuspid valve combined with valve valvular lesions in children, combined with cardiac ultrasound, enhanced CT, postoperative follow-up thrombin time (PT) and international standardized ratio (INR) and related literature sharing learning.
Results The child, male, 2 years old and 8 months old, more than 2 years after complex congenital heart surgery, the child underwent aortic valve, tricuspid valve and pulmonary valve plasty under general anesthesia. Strengthening skin and body position care after surgery is conducive to pericardial pleural effusion excretion and lung dilatation. Monitor the built-in length of tracheal intubation and record that the temperature of the ventilator humidifier is maintained at 32-37 ° C, the negative pressure of sputum absorption is ≤-300mmHg (≤-0.04Mpa) to reduce damage to the vascular wall, and use Oprilin hydrochloride, adrenaline and noradrenaline to improve cardiac diastolic and contraction, cardiac discharge The blood volume gradually increases, and the hypocardiac excretion state gradually improves. Children take warfarin orally according to the doctor's advice, cooperate with heparin sodium vein maintenance treatment, daily detection of thrombin time (PT) and international standardized ratio (INR) to adjust warfarin dose, children wake up after surgery and give Wiku ammonium bromide and imidazoleamine intermittent use, right meto Midine maintains sedation, reduces oxygen consumption, and reduces the metabolic burden of various organs. Evaluate to avoid respiratory depression caused by excessive sedation, shorten mechanical ventilation time, and reduce the incidence and fatality of acquired delirium. Giving early enteral nutrition to children can promote the secretion of digestive tract hormones and the recovery of intestinal mucosa, achieve the target feeding amount, and promote postoperative recovery.
The child successfully completed aortic valve tricuspid valve plasty. Through postoperative fine, individualized and specialized nursing management, the postoperative hemodynamic stability was maintained, and the left ventricular ejection fraction (LVEF) was regularly reviewed by >46% and LVEF was ≥63%. There were no postoperative complications. Game counseling was invoked during the treatment period to reduce isolated anxiety. By guiding the family members of home care, the quality of continuous care and family members's hospitalization satisfaction was improved.
Conclusion Cardiac combined valve lesions are more important in children's congenital heart disease. It is necessary to strengthen the postoperative refinement and high-quality nursing of children, improve the quality of life after surgery, strengthen the screening of congenital heart disease in children, and improve the quality of the birth population.

关键字 heart combined valve; postoperative monitoring; nursing; children

分类：19. Nursing 护理
955

Advances in research on the status of transition readiness services for children with epilepsy to adulthood

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Epilepsy is one of the most common chronic neurological disorders in children, and epidemiological surveys in China show that the prevalence of epilepsy ranges from 4% to 7%, with approximately 75% of patients having an onset in childhood, while 50% of seizures and treatment will accompany them into adulthood. The transition from adolescence to adulthood with chronic disease is considered a critical and challenging process. The complexity of epilepsy, recurrent seizures, and prominent co-morbidities place a heavy burden on families and society, and the collision of the transition phase with adolescence increases the vulnerability of the process, which is susceptible to multiple factors such as the disease itself, health system services, and family, resulting in poor health-related outcomes and psychosocial development This can lead to poor health-related outcomes and impaired psychosocial development, affecting the growth and social survival of the child. Adequate transition preparation improves adverse health outcomes, reduces emergency department visits, increases adherence to treatment, and reduces the risk of morbidity and mortality. As medical technology advances, the quality of life and life expectancy of children with chronic diseases have increased, and more than 90% of adolescents with chronic diseases survive into adulthood requiring Health Care Transition (HCT) services. The Health China 2030 and the China Child Development Program issued by the State Council of the central government of China emphasize the establishment and implementation of continuous, full-cycle health services and referral services for children and their adolescents. A unified standard transition readiness intervention program for adolescents with chronic diseases has not been established in China, and it is necessary to review and analyze the relevant literature in this field. In this paper, we review the factors influencing transition readiness, assessment tools, care protocols, and outcome indicators for adolescents with epilepsy, explore the characteristics and difficulties of transition care interventions for this group, and propose localized service strategies for transition readiness of adolescents with chronic illnesses in the context of China's national situation, with the aim of providing informative suggestions for improving transition readiness of this group, facilitating their smooth transition to the adult healthcare system, and improving the quality of life of adolescents with epilepsy and families. The aim is to provide a more accurate health service strategy for medical institutions in China to implement comprehensive transition management and life-cycle support for children with chronic diseases.

关键字 Key words：Epilepsy；Adolescents； Transition readiness ； Summary ;Nursing

分类：19. Nursing 护理
966

Pharmacological and Non-pharmacological Interventions in Management of Peripheral Venipuncture related Pain: A Randomized Clinical Trial

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Abstract
Aim: To evaluate whether an integration of pharmacological and non-pharmacological interventions is more effective than either one of intervention in pain reduction during pediatric peripheral venipuncture(PVP).

Design: A randomized controlled trial (RCT) with three parallel groups was performed in the respiratory and gastroenterology ward of Children's Hospital of Fudan University.

Methods: A total of 299 children aged 3-16 years old were recruited between 4 February, 2019 to August, 2020. Participants were randomized into three groups: EMLA group(n=103), distraction group(n=96) and combined group(n=100). The intravenous cannulation(IVC) was performed in all group of children. Children in EMLA group were applied EMLA cream on the pre-venipuncture site before 30 minutes of PVP, while those in distraction group were allowed to play distraction toys with game therapist before 5 minutes of PVP. Children in combined group were applied EMLA cream for 30 minutes and then play distraction toys with nurse for 5 minutes before PVP. The game therapist was assigned to distract children's attention throughout the whole process of PVP using distraction tools in distraction group and combined group. The level of pain and stress of children during PVP were rated and measured.

Results: All three intervention groups responded with light pain during PVP by both the Wong Baker rating scale(WB) and revised-FLACC pain scales (r-FLACC). Additionally, the difference of stress measured by salivary cortisol of distraction group and combined group is significant (P=0.013), children in distraction group shown lower stress than those in combined group. Other physiological findings including heart rate, oxygen saturation(SPO2), and venipuncture related data including puncture duration and retain time of intravenous cannula of the three groups are not statistically significant.

Conclusions: All three interventions decrease venipuncture pain, but distraction techniques alone have shown to elicit lower stress response than combined distraction with EMLA. Considering the time and cost, distraction techniques are the most highly recommended in managing venipuncture pain in the pediatric ward.

Impact: The finding of this study can be a reference in implementing pain reliving interventions and choosing age-appropriate distraction tools for clinical nurse in managing needle-related pain and stress.

关键字 Venipuncture pain, EMLA cream, distraction techniques, nursing

分类：19. Nursing 护理
970

A nurse-inserted Peripherally Inserted Central Catheter program in General Pediatrics: A single center experience

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Abstract
Objective To share the experience of a nurse-inserted peripherally inserted central catheters (PICC) program initiated in a general pediatric department.
Method This is a retrospective descriptive study based on prospectively collected data. All PICCs inserted in the departments of gastroenterology and pulmonology in a tertiary pediatric center from Dec. 2015 to Dec. 2019 were included in the study. Complications and risk factors were analyzed through comparing cases with and without complications. We also reported arm movements in malpositioned PICC corrections.
Results There were 169 cases with median(IQR) age of 42(6, 108) months received PICC insertion during 4-year period. Inflammatory bowel disease was the leading diagnosis accounting for 25.4%(43/169) of all cases. The overall complication rate was 16.4 per 1000 catheter days with malposition and obstruction as the two most common complications. Multivariate models performed by logistic regression demonstrated that young age [p=0.004, OR(95%CI) = 0.987(0.978, 0.996)] and small PICC diameter (1.9Fr, p=0.003, OR(95%CI) = 3.936(1.578, 9.818)] were risk factors for PICC complications. Correction of malpositioned catheters was attempted and all succeeded in 9 eligible cases by using arm movements.
Conclusion The nurse-inserted PICC program is feasible in general pediatrics with low complication rates. PICC tip malposition and obstruction were two major PICC-related complications with young age and small catheter lumina as risk factors. Arm movement can be used to correct the malpositioned PICC catheters.

关键字 Peripherally inserted central catheter; pediatrics; malposition; complication, arm movements

分类：19. Nursing 护理
971

he nursing management of Anastomotic dehiscence after Ileostomy closure: A case study of an infant with severe undernutrition and peristomal irritant dermatitis

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ABSTRACT
Anastomotic dehiscence (AD) is a costly post operate complication in which the anastomotic stoma fails to heal and ruptures along a surgical incision. This case study presents the whole process of wound healing and discusses why the AD occurred after the ileostomy closure and how nutrients enhanced the healing process. Additionally, we would like to remind people that patient's status of nutrition and peristomal skin should be fully considered before performing the surgery of stomal closure, poor nutrition status and severe peristomal skin damage are likely to result in AD.

关键字 Anastomotic dehiscence ileostomy closure Nutrition Peristomal irritant dermatitis Wound healing

分类：19. Nursing 护理
986

Psychological Processes and Coping Styles of Primary Caregivers of Children with Biliary Atresia in China a Single Center: A Qualitative Study

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Aim: To explore the psychological processes and coping styles of primary caregivers of children with biliary atresia (BA) in a single center in Shanghai.
Methods: A qualitative study, based on grounded theory, was conducted in a Grade-A children’s hospital in Shanghai. Face-to-face, semi-structured interviews were conducted from September to November 2020 with 10 primary caregivers who cared for children with biliary atresia. All interviews were recorded, transcribed, and analyzed using continuous comparative data analysis.
Results: Analysis of the collected data revealed complex psychological processes of primary caregivers during the care of children with biliary atresia. Caregivers showed different psychological states and coping methods before diagnosis, after diagnosis, postoperative stage, and discharge stage. The psychological states in each stage were affected by many factors, all of which were related to the coping methods used. All these factors jointly affected the psychological changes of primary caregivers. Caregivers demonstrated complex emotions before the diagnosis of the disease. After diagnosis, negative emotions appeared. In the postoperative stage, positive emotions gradually increased. Both positive and negative emotions coexisted following discharge.
Conclusions: The study provides a better understanding of the psychological processes and coping methods used among primary caregivers of children with biliary atresia in the various stages of the disease. Identifying the demands of the primary caregivers can lead medical staff to carry out effective strategies to help caregivers adapt to the psychological changes.

关键字 biliary atresia; caregiver; psychology; coping; qualitative study

分类：19. Nursing 护理
992

Nursing of subclavian artery-pulmonary artery shunt after separation of thoraco-umbilical conjoined twins

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Objective: Siamese twins are the result of abnormal embryogenesis, with an incidence of about 1 in 50,000. Tetralogy of Fallot (Tof) is the most common cyanotic congenital heart disease, and most patients have dyspnea after birth. Early detection, early diagnosis and early treatment are of great significance for improving the survival time and quality of life of patients.The main treatment for these patients is surgery. Through the study of a case of thoraco-umbilical conjoined twins undergoing subclavian artery-pulmonary artery shunt after separation, the corresponding nursing measures and their quality were discussed.
Methods: The elder daughter of a pair of conjoined twins with tetralogy of Fallot was selected. The baby was admitted to the hospital two hours after birth because of ″conjoined twins″. He was connected with another fetus from two centimeters below the nipple to the umbilical cord. He shared the liver with the younger daughter. The arrangement of large blood vessels was abnormal, which was consistent with tetralogy of Fallot. The indication of operation was determined.After the exclusion of surgical contraindications, unequal separation of conjoined twins and BT shunt were performed.
Results: After the separation of conjoined twins and before BT shunt: 1. Temperature monitoring, the temperature regulation center and physiological function of infants were not fully developed, the skin wound was large after the separation, and the loss of heat and water was accelerated. An infrared radiation warm-keeping table is use for keeping warm, that head and the limb are wrapped by disposable paper diapers, and the radiation table is cover by a disposable preservative film; The skin temperature probe monitors the change of body temperature,Concentrate on the operation to reduce the skin exposure time of children. 2. Organ function monitoring showed that the liver injury was serious after separation. The changes of sclera, skin, urine and stool color were observed, and the liver function indexes were monitored. 3. Wound care. After thoraco-umbilical separation, the abdominal volume became smaller and the tension increased. Observe whether there was increased intra-abdominal pressure and bleeding.After operation, the wound was bandaged with abdominal belt and the abdominal wound was cleaned regularly. After BT shunt: 1. Cardiac function monitoring, artificial blood vessel connection and anastomosis are prone to blockage or bleeding, percutaneous oxygen probe monitoring of blood oxygen after operation, invasive blood pressure device monitoring of arterial blood pressure, and positive inotropic drugs to enhance myocardial contractile function according to doctor's advice. 2. Respiratory system management,After the operation, the pulmonary perfusion blood flow increased and the pulmonary exudation changed, and the positive airway pressure was maintained by a ventilator. Dexmedetomidine hydrochloride continued sedation after operation to prevent restlessness and increase myocardial oxygen consumption after awakening. 3. Nursing of drainage tube, one drainage tube was placed after BT shunt, the drainage tube was properly fixed, marked, connected to the negative pressure suction device, and squeezed regularly.Keep the pericardial and thoracic drainage tube unobstructed, observe and record the color, quality and quantity of drainage fluid. Active bleeding should be detected in time to avoid the blockage of drainage pipes and the occurrence of pericardial tamponade. After treatment and nursing, the

patient was transferred to the general ward 14 days after the shunt operation and discharged 20 days later.
Conclusion: High quality nursing measures can increase the survival rate of children after operation.

关键字 Conjoined; Congenital; BT shunt; Nursing Care

分类：19. Nursing 护理
1067

Nursing treatment of subcutaneous hemorrhage after blood collection in a patient diagnosed with systemic lupus erythematosus complicated with renal failure underwent hemodialysis

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Objective: To explore the nursing treatment of large area subcutaneous hemorrhage in forearm caused by venous blood collection in a patient diagnosed with systemic lupus erythematosus complicated with renal failure underwent hemodialysis.
Methods: Clinical data of a patient diagnosed with systemic lupus erythematosus complicated with terminal kidney treated in our hospital in 2020 was reviewed, through local pressure and prolongation of pressing time, local pain relief and wound nursing were given according to NRS pain digital score , potato chips and Xiliaotuo were applied to the bruises, and infrared physiotherapy was used to observe the effect after the implementation.
Results: A patient diagnosed with systemic lupus erythematosus complicated with terminal kidney was admitted to our department in 2020, hemodialysis was performed, 30 minutes after dialysis, blood samples were collected from the median elbow vein and local routine compression was performed. Subcutaneous ecchymosis 4*5cm could be seen at the puncture site 3.5h later, Pressure hemostasis was given and local bleeding was alleviated after hemostasis with elastic bandage. After 19 hours, an 1*1cm ulceration could be observed in the skin, The diameter of ecchymosis increased to 6 × 14 cm. Then the area of pressing site was increased, the pressing time was prolonged, silver ion alginate dressing was used in the ulceration , and potato chips, Xiliaotuo was applied and infrared physiotherapy were used in the bruises. 3 days later, the NRS pain score decreased from 6 points to 2 points, and the eschar shell fell off 6 days later. during follow-up, the ecchymosis of the arm disappeared 20 days later.
Conclusion: Local routine pressing is not suitable for patients after dialysis. Venipuncture should be avoided or delayed at the end of dialysis. When venipunctureis needed, experienced nurse should carry out the operation, and correct finger pressing should be applied and the pressing time should be belonged. Xiliaotuo and Potato chips can be given in subcutaneous bleeding, infrared physiotherapy and ion alginate dressing can be performed in broken wound ,promote exudate absorption and wound healing.

关键字 Hemodialysis, venous blood collection, subcutaneous bleeding

分类：19. Nursing 护理
1078

The application of innovative "happy ward" working mode in pediatrics

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Methods: By optimizing children's medical treatment and admission, and using 6S scientific management mode, animation element cartoon ward, children's personalized graffiti area and picture books borrowing services. At the same time, through the "pediatric nursing team culture display wall", "nursing star", and the "five-star evaluation method" is adopted for department nursing work.In terms of management, establish a continuous supervision mechanism, set every Friday as the "Head Nurse Listening Day", and carry out all kinds of group building activities regularly to increase team cohesion.Results: After the implementation of this model, it enhanced the trust of patients' family members, improved the satisfaction of nursing service, and further improved the level of quality pediatric nursing service. At the same time, department nurses also learned to enjoy the happiness of work, so that nursing disputes were significantly fewer and complaints.Conclusions: To sum up, innovating the working mode of "Happy ward" has constructed a harmonious patient care relationship by reducing patients' medical treatment tension and anxiety, improving the quality of nursing service and deepening the connotation of quality service.

关键字 Happy ward; pediatrics; nursing; satisfaction

分类：19. Nursing 护理
1148

Nursing care of 22 infants with severe pertussis

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Objective To summarize the nursing care of 22 infants with severe pertussis. Methods Comprehensive nursing care nursing evaluation, symptom recognition and nursing, nutritional support, drug care and vaccination guidance can promote the rehabilitation of 22 infants with severe pertussis. Result After active treatment and nursing, 22 infants with severe pertussis had been cured .Conclusion Children’s pertussis is mostly transmitted in the family, and it has the characteristics of low onset age, severe symptoms, many complications and long treatment time. Through effective treatment and nursing, children with pertussis can recover .At the same time, it is suggested that the infection rate of adults can be controlled by increasing the vaccination rate of women of childbearing age, thus reducing the incidence of pertussis in infants.

关键字 pertussis; severe infection; infant; nursing

分类：19. Nursing 护理
1150

Vaccines for varicella and herpes zoster in secondary immunocompromised children with severe varicella Discussion on inoculation

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Through the clinical evaluation and analysis of 91 children with secondary immunocompromised and severe varicella from 2015 to 2020, it was found that once the immunocompromised children contracted varicella, their clinical symptoms were more severe than ordinary varicella, the course of the disease was longer, and its basic nature was aggravated at the same time. The condition of the disease. Based on the epidemiology of this group of children, this article suggests that immune-compromised children should be vaccinated with varicella vaccine at the right time and caregivers in their families over 50 years of age should be vaccinated with herpes zoster vaccine, which can reduce the risk of varicella infection in such children.

关键字 immunocompromised; children; severe varicella; varicella vaccine; herpes zoster vaccine

分类：19. Nursing 护理
1181

Nursing care of a child with refractory epilepsy and feeding difficulties combined with central respiratory failure

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To summarize the nursing points of a child with refractory epilepsy and feeding difficulties combined with central respiratory failure.The main points of care include: medication and care of refractory epilepsy and monitoring of complications, care of venous access to prevent tube blockage; strengthen the airway management of children, regularly carry out tracheotomy and surrounding skin assessment, maintenance and prevention of complications to ensure unobstructed airway of the child and reduce the incidence of complications; maintain the gastrostomy tube and surrounding skin regularly to reduce complications, keep the pipeline unobstructed, and ensure the child’s nutritional intake; choose targeted infection control measures to improve the infection of children cooperate with the rehabilitation department to carry out the early stage of the child Rehabilitation treatment to prevent the occurrence of ICU acquired weakness of the child; to assess the child’s readiness for hospital discharge, to train the caregivers and improve the caregivers' home care ability. After 79 days of cooperative treatment and care by a multidisciplinary team, the child recovered well, his vital signs were stable, and his weight increased to 14.5Kg, and he was discharged from the hospital.

关键字 Refractory epilepsy; Feeding Difficulties; Central Respiratory Failure; Tracheostomy; Percutaneous Endoscopic Gastrostomy; Pediatric Nursing

分类：19. Nursing 护理
1206

Status and influencing factors of Participation behavior in healthcare during transition period with epilepsy adolescents: A cross-sectional study in China

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Purpose: The present study investigated the degree of participation in healthcare behavior by Chinese adolescents with chronic epilepsy and identified factors that should be addressed by health interventions.
Methods: The study used a convenience sample of 1238 adolescent patients with epilepsy, who were hospitalized in 17 tertiary A-level children or maternal and child specialty hospitals in China between January 2017 and March 2020. Several scales were used to measure their degree of participation in healthcare behavior and the factors that influence it. Data collection was conducted after uniform training of the investigators. The adolescents who met the inclusion and exclusion criteria could scan the QR code of the questionnaire via a mobile phone.
Results: The age of the participants ranged from 12.2 to 17.8 years (mean 14.2 years), and the sample had a male-to-female ratio of 1.25:1. The patients' average total score of participation in healthcare behavior was 125.58 (SD = 12.25), which was lower than the norm for China. Their scores on the six dimensions of participation were highest for information interaction, followed in descending order by medical decision[1]making, treatment and care, appeal, diagnosis and treatment decision-making, and questioning supervision. Multiple linear regression found significant associations between health-care participation and five personal and disease variables (gender, age, course of disease, number of comorbid diseases, type of family structure), self-effificacy, and coping styles (cognitive-palliative and acceptance), which explained 52.1% of the variance in patients' total scores on participating in healthcare behavior.
Conclusions: The participation of young Chinese patients with epilepsy in transitional healthcare behavior needs to be improved. Participation was positively associated with being female, a longer course of disease, fewer comorbidities, and living in a nuclear family. Patients who used cognitive-palliative and acceptance coping styles and those who had higher self-effificacy also had signifificantly higher levels of participation in healthcare behavior. The study provides useful reference points for adolescents with chronic disease to participate in healthcare programs.

关键字 Adolescent; Epilepsy; Child to adult transition period; Participation in health care behaviors; Social support; Influencing factors

分类：19. Nursing 护理
1229

Evidence summary on maintenance and management of neonatal umbilical catheterization

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Objective To retrieve the evidence for the maintenance and management of neonatal umbilical catheterization at home and abroad, and to evaluate and summarize the best evidence. **Methods** Systematic search of UpToDate, BMJ clinical evidence, NGC, SIGN, GIN, NICE, NANN, China Clinical Guidelines Library and other web pages，PubMed, EMBASE, Central, CINAHL, Cochrane Library, China Biomedical Documentation Service System, CNKI, Wanfang Data, Weipu and other databases regarding all the evidence on the maintenance and management of neonatal umbilical catheterization, the search time limit is to build the database until April, 2021. Two researchers evaluated the quality of the included literature, and extracted evidence from the literature that met the quality standards. **Results** A total of 13 articles were included, and 19 best evidences were collected from 6 aspects including the method and location of umbilical catheterization, catheter depth, catheter selection, catheter device management, catheter removal timing, and prevention and control of complications. **Conclusion** This study provides clinical medical staff with evidence-based evidence for the operation and maintenance of umbilical catheterization. which can promote the standardized management of neonatal umbilical catheters and reduce the incidence of related complications.

关键字 neonates; umbilical catheters; complications; best evidence; evidence-based nursing

分类：19. Nursing 护理
1236

Medicine safety research on current situation of knowledge-attitude-practice in neonatology nurses and management strategy recommended in Sichuan

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Objective：Medicine safety is a topic of global concern, being the risk of hospital management. As the key personnel of medicine management and administration, nurses should master solid theoretical knowledge, form good belief and implement medicine safety administration measures. The purpose of this study was to explore the current situation of knowledge-attitude-practice in evaluating the medication safety of neonatal nurses in Sichuan province, to understand situation of nurses' knowledge-attitude-practice on medicine safety in neonatal department, and to analyze the influencing factors leading to the difference of medicine safety knowledge-attitude-practice among them. Then management strategy was put forward for medicine safety of nurses.
Method：Through literature review and Delphi method was used to develop and construct a questionnaire on knowledge-attitude-practice of medication safety for nurses in neonatal department. After a small sample pre-survey, the formal questionnaire was determined. A total of 773 neonatal nurses from 129 hospitals in Sichuan Province were investigated. The questionnaire consisted of general demographic data, administration of medicine and forms on knowledge-attitude-practice of medicine safety. The results of the survey were analyzed by SPSS 21.0 software respectively. The general data were described by mean, standard deviation and composition ratio, and the factors influencing the knowledge-attitude-practice were analyzed by single factor, t-test, multiple stepwise regression and pearson correlation analysis.
Result：1.The self-developed questionnaire of knowledge-attitude-practice on medicin safety of nurses in neonatal department was constructed through two rounds of experts' inquiries. The authoritative coefficient was 0.97, the expert positive coefficient was 100%, and the Kendall harmony coefficient was tested, P<0.001. 2. The total score of knowledge-attitude-practice on medication safety of nurses in neonatal department in Sichuan province was 127～212, with an average score of 189.27. The full score of the knowledge part was 34, with an average score of 23.15 ± 3.962; the full score of the attitude part was 55, with an average score of 51.21 ± 5.504; the full score of the practice part was 125, with an average score of 114.91± 8.770. 3. Multivariate linear regression analysis showed that the working years in neonatal department, the positions of nurses, hospital level, the participation of pharmacists in drug guidance, the convenience of inquiring information and the knowledge regression equation of two-level training both department and hospital had impact on the situation of knowledge mastery. The attitudinal regression equation was used in the drug conversion table, which affected the attitude/belief of neonatal nurses; different ages, the educational background, two-level training, convenient information for inquiring and the behavior regression equation was used in the drug conversion table, which affected the behavior on medicine safety of neonatal nurses. 4. The knowledge and attitude, attitude and practice, knowledge and practice of nurses in neonatal department had significant correlation. The correlation coefficient r ranged from 0.281 to 0.386, all P<0.001.
Conclusion：1. The self-developed questionnaire with good reliability and validity can be used as an evaluation tool for evaluating the situation of nurses'

knowledge-attitude-practice on medication safety in neonatal department. 2. The attitude dimension of nurses in neonatal department of hospitals in Sichuan Province was good, but their knowledge level was poor, and the practice part needed to be improved. 3. We should strengthen the training of medication safety knowledge for neonatal nurses, consolidate the attitude/belief of medication safety, improve the behavior of implementing medication, and promote the medication safety management in neonatal department.

关键字 medicine safety; knowledge-attitude-practice; neonatology; nurses

分类：19. Nursing 护理
1241

Nursing progress of extracorporeal membrane oxygenation (ECMO) in neonates

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Objective: To review the nursing progress of extracorporeal membrane oxygenation (ECMO) in neonate and provide guidance for caring neonates during ECMO therapy. Methods: PubMed, EMBASE, Wanfang and CNKI databases were retrieved to collect relevant studies on nursing of ECMO therapy. Results: ECMO system related management includes management of circuit, monitor of the blood flow and pressure, and common machine failure handling. Patients related management includes monitor of hemodynamics, temperature, and complications, management of ventilation, nutrition support, infection prevention, positioning. Conclusion: ECMO provides an effective way for newborns who have failed to respond to conventional respiratory support. Nursing patients supported by ECMO patients is difficult due to the critical illness of newborn needing ECMO support, the complex ECMO circuit, and the rapid change of newborn's illness. The focus of care for patients with ECMO is on the care of the ECMO circuit and monitoring the response of the newborn during procedure.

关键字 extracorporeal membrane oxygenation, respiratory failure, newborn, nursing

分类：19. Nursing 护理
1242

The influence of bathing methods on body temperature in premature infants: a systematic review

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Objective：To systematic review the different bathing methods on body temperature of premature infants. Methods:PubMed, Embase, the Cochrane Library, CINAHL, CBM, WanFang and CNKI databases were retrieved to collect studies on bathing methods for premature infants. Revman and GeMTC software were used for meta-analysis and network meta-analysis. Results: A total of 5 studies were included, involving 348 preterm infants. Meta-analysis showed that there was no statistically significant difference in body temperature between swaddled bath and tub bathing [MD=0.23, 95%CI(-0.21,0.67), P>0.05]. Compared with tub bathing or swaddled bathing, the premature infants had significant lower body temperature after sponge bathing[MD=-0.15, 95%CI(-0.23,-0.07), P<0.05; MD=0.39, 95%CI(0.31,0.47), P<0.05].The rank probability of network meta-analysis showed that swaddled bathing was the best way to maintain the body temperature of preterm infants, followed by tub bathing, followed by sponge bathing. Conclusion: Swaddled bathing and tub bathing were better than sponge bathing in maintaining the body temperature of premature infants. Swaddled bathing can be the first choice for premature infants.

关键字 premature; baths; swaddled bathing; sponge bathing; systematic review

分类：19. Nursing 护理
1243

Meta-analysis of influencing factors of neonatal PICC-related phlebitis

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Objective: To explore the influencing factors of neonatal PICC-related phlebitis. Methods: PubMed, EMbase, CENTRAL, CINAHL, CBM, wanfang and CNKI databases were retrieved to collect domestic and foreign studies on influencing factors of neonatal PICC-related phlebitis. Revman 5.3 and GeMTC software were used for meta-analysis and network meta-analysis. Results: A total of 32 studies were included, including 15 RCTs, 2 case-control studies, and 16 cohort studies, involving a total of 8278 children. Meta-analysis results showed that the influencing factors of neonatal PICC-related phlebitis were catheter ectopic [OR=5.53, 95%CI (1.22, 25.15)], catheter blockage [OR=7.18, 95%CI (3.54, 14.56)], gestational weeks [OR=2.51, 95%CI (1.35, 4.66)], dexamethasone preinfiltrating catheter [OR=0.26, 95%CI (0.17, 0.41)], and innovative nursing intervention [OR=0.17, 95%CI (0.07, 0.42)]. Network meta-analysis results showed that compared with lower limb vein, scalp vein [OR=3.57, 95%CI (1.39, 10.18)] and upper limb vein [OR=1.89, 95%CI (1.08, 3.37)] has a statistically significant difference in the incidence of phlebitis, while there was no statistically significant difference in the incidence of phlebitis between scalp vein and upper limb vein [OR=0.53, 95%CI (0.20, 1.26)]. Conclusion: Catheter ectopic, catheter blockage and small gestational week were risk factors for PICC-related phlebitis, while dexamethasone preinfiltrating catheter and innovative nursing intervention were protective factors for PICC phlebitis. Venipuncture of lower limbs is the most likely to cause phlebitis.

关键字 newborn; PICC; phlebitis; influencing factors

分类：19. Nursing 护理
1276

Construction and application of training system for new nurses in neonatology department based on onion model

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Objective Based on the onion model, a training system for newly recruited neonatologists was constructed and its application effects were discussed. Methods A teaching management team was established. Based on the theoretical framework of the onion model, a training system for newly recruited nurses in the neonatology department was constructed using literature research and semi-structured interviews, and applied to the training of newly recruited nurses in the neonatology department from March 2020 to February 2021. , Adopting a concurrent control design, the experimental group adopts the training system based on the onion model for training, and the control group adopts the conventional training method. During the training period, monthly evaluation of the training target's theory, operation, and clinical performance of the patients in charge. And use the t test of two independent samples to compare the differences in the performance of the two groups. Results The theoretical scores of the experimental group and the control group were 95.77±2.93, 93.99±1.79; the operating scores were 95.86±2.86, 94.60±1.41, and the differences were statistically significant (P<0.05). The clinical scores of patients in charge were 95.10±3.29 and 94.20±2.03, and the difference was not statistically significant (P>0.05). Conclusion The training system for newly recruited neonatologists based on the onion model can improve the professional quality of newly recruited nurses and the ability of clinically in charge of patients, and at the same time improve their theoretical and operational performance. It is worthy of clinical application.

关键字 Onion model; neonatology; nurse; training

分类：19. Nursing 护理
1277

Effects of symptom assessment method on the training of new nurses in neonatal intensive care unit

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Objective: To explore the effects of symptom assessment method in the training of new nurses in neonatal intensive care unit.
Methods: Based on the disease assessment framework, the training program of symptom assessment was developed and applied. Evaluating the training effects through knowledge level assessment and practice reports.
Results: A total of 34 new nurses completed the training. The difference of knowledge level assessment scores before and after training was statistically significant (t =14.699, p =0.000). Of the 34 practice reports on symptom assessment, 88.24% scored above 80, with a median score of 89. The result of quality evaluation after teaching shows overall satisfaction.
Conclusion: Symptom assessment method can help to improve the theoretical and practical assessment level of nursing staff, and obtain very satisfactory training effect, which is worth promoting.

关键字 NICU, Nurse, Inservice Training, nursing education, symptom assessment method

分类：19. Nursing 护理
1443

Evidence-based perioperative feeding strategy shortened fasting time for non-gastrointestinal surgical pediatric patients

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Aim: Minimize the fasting time perioperatively of surgical children can enhance their postoperative recovery. However, there are factors in clinical setting that severely prolong the fasting time before and after surgery. Under this background, we built a perioperative feeding strategy under methodology of evidence-based nursing, combined with an operation proceed monitoring system, and then used it on the general surgery department for testing its safety and efficacy.

Methods: A quasi-experiment design was used. After the ethics committee approval and with parental informed consent, planned non-gastrointestinal surgical patients aged 6-month to 14-year were enrolled.The study included 168 children with control=84 and intervention=84. The control group was allowed 8 hours for fasting solid food and 2h for fasting water, postoperative refeeding water begin 2h after returning from PACU, gradually transitioned to milk or porridge on the surgery day, and to normal feeding on post-operation day 1. The intervention group received dynamic adjustment for preoperative clear liquids fasting depending on the whole operations proceed, for which was shown on a hospital operation proceeding system. Once the child recovered from anesthesia (Steward scale for evaluating if the child has awakened), he or she was allowed early postoperative oral intake using a straw, transition to semi-solid food 15 minutes afterwards, and to normal feeding 30 minutes afterwards if the child has no nausea or vomiting. Data collection tools include the Post-Anesthesia Emergence Delirium scale, Visual Analogue Scale for thirst and hunger rating and Wong-Baker face scale used for pain rating for children over 3-year, crying times for thirst and hunger rating and FLACC used for pain rating for children under 3-year. The actual pre- and postoperative feeding time and kinds of food or liquids of patients were documented by a research nurse, and the time points of anesthesia and surgical began and finished was obtained from the hospital medical system. The descriptive statistical analyses of the quantitative variables were performed using the mean±standardized difference or median(P_{25},P_{75}) depending on if the data obey normal distribution. Count data were expressed in terms of frequency or rate, and analyzed using the Chi-square test, Fisher exact test or Mann-Whitney U test. Measurement data with a normal distribution were analyzed using *t* test (independent samples).

Results: A total number of 168 children were enrolled in this study with complete data. The demographics data and surgery area of the patients included in the final study dataset showed no significant differences, with age (P=0.801), gender (P=0.322), and surgical area (P=0.408). All children followed general anesthesia. The actual preoperative fasting time for clear liquids of intervention group were 4.38(2.91,9.79) hours versus 5.26(4.12,8.08) hours of control group (P=0.028). Postoperatively, the actual refeeding time for clear liquids of intervention group were 0.25(0.01,0.68) hours versus 2.08(2.0,2.23) hours of control group (P<0.001), and the actual refeeding time for semi-solids of intervention group were 0.83(0.50,1.42) hours

versus 2.83(2.42,3.79) hours of control group (P<0.001). When children returned from PACU to ward, rate of post-anesthesia emergence delirium was 2(2.38%) in intervention group versus 27(32.14%) in control group (P<0.001). Pain level within 1h postoperatively of the intervention group was significantly lower than control group (P<0.001). Rate of nausea and vomiting within 1h postoperatively was no statistically significant between groups (P=0.484).

Conclusions: This study provided evidence that using operation proceed monitoring system to dynamically adjust the clear liquids fasting time points and administering oral hydration at early postoperative time points were safe and feasible in those children in a clinical ward setting, improving comfort and decreasing thirst.

关键字 evidence-based; perioperative; feeding; children

分类：19. Nursing 护理
1489

Bibliometric study on Chinese massage in the treatment of pediatric diarrhea

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Objective: To analyze the current situation and problems in the application of traditional Chinese medicine massage in pediatric diarrhea, so as to provide a reference basis for related research in this field.
Methods: The research literature on the treatment of pediatric diarrhea by massage in Chinese medicine published in China National Knowledge Infrastructure(CNKI), Wanfang Database, Chinese Medical Journal Database(CMJD), and China Biology Medicine disc(CBMdisc) from May 1, 1965 to August 26, 2021 were searched, and the basic situation, design methods and the results were systematically analyzed by bibliometric methods.
Results: A total of 75 literatures were included and published in 40 journals, including 31 case studies and 44 randomized controlled trials (RCT).
Among the 44 randomized controlled literatures, only 12 literatures were grouped by the randomized numerical table method, and 22 literatures did not explain the specific grouping method. The first author comes from originated from 13 articles (17.3%) in Central China, 10 articles (13.3%) in North China, 30 articles (40.0%) in East China, 6 articles (8.0%) in South China, 3 articles (4.0%) in Northwest China, 5 articles (6.7%) in Northeast China and 8 articles (10.7%) in Northeast China. The total sample size of the study was 8472 cases; the age of the subjects ranged from 1 month to 6 years, with an average age of (2.24±0.47) years. The duration of the disease ranged from 3~60 days, with an average duration of (16.25±10.60) days. According to the dialectical typology, 22(29.3%) of the acupoints and techniques were selected; the basic acupoints and techniques were selected first, and then the dialectical addition and subtraction accounted for 14(18.7%); 39(52.0%) were not dialectical classification, and only special techniques were used. The commonly used massage techniques were kneading, pushing, kneading and rubbing，other techniques as a complementary technique. The rubbing method was divided into clockwise needle rubbing and counterclockwise rubbing, counterclockwise rubbing was tonic, and clockwise rubbing was diarrhea. The massage time was 2~5 minutes, with an average time of (3.58±1.25) minutes. The massage frequency of each acupoint was 100~500 times, with an average of (234.58±111.30) times. The massage course is 3~10 days, with an average course of (5.34±1.73) days. The evaluation index of massage in the treatment of pediatric diarrhea is mainly the evaluation of TCM syndrome efficacy, and the treatment efficiency was more than 90%.
Conclusions: Chinese massage has obvious effect in the treatment of pediatric diarrhea,at present, although there are many relevant studies, tthere are no unified quantitative standards for pediatric massage acupoints, frequency, time and course of treatment. At the same time, and the quality of the literature is generally not high due to the limitation of the sample size and design of the studies, which need to be verified by multicenter, large sample and high-quality randomized controlled trials.
Keywords: Massage, Pediatric Diarrhea, Literature analysis, Bibliometrics

关键字 Tui Na, Diarrhea, Literature analysis, Bibliometrics

分类：19. Nursing 护理
1794

An Overview of Omics-based Research Led by Nurse Scientists

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Objective: The purpose of this article was to provide an overview of the multiple branches of omics in nursing research.
Methods: We performed a systematic search via PubMed and Web of Science published from earliest to July 2021. Papers with at least one of the authors was a nurse could be included.
Results: The search produced 4016 records to be analyzed. Publication dates of the reviewed papers spanned the years from 2001 to 2021. The themes, objects and study design varied in nurse-led omics studies. Among all omics technologies, genomics, epigenomics and metabolomics were most commonly used by nurse scientists.
Conclusion: In the continual contribution to safe and effective precision health care, it is vital to integrate omics content into nursing research and education.

关键字 Nursing, Omics

Category: 19. Nursing 护理
1729072

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Abstract Content Objective To analyze the methods and effects of clinical monitoring and comprehensive nursing for severe pneumonia in children.Methods 84 cases of severe pneumonia in children were treated in our hospital in Octobeer -2019 in May 2019. The patients were divided into reference group and 42 cases in the study group. The patients were given routine nursing, clinical monitoring and comprehensive treatment. Nursing intervention. Observe and compare the pulmonary function monitoring index and nursing satisfaction score of the two groups. Results the recovery time of cough, fever, and shortness of breath in the study group was earlier than that of the reference group and the nursing satisfaction score of the study group. The total effective rate was higher than the reference group (P < 0. Five. Conclusion Clinical monitoring and comprehensive nursing can shorten the time of symptom recovery, improve the pulmonary function and respiratory function, shorten the hospitalization time of the children, and it is worth popularizing.

Key words keywords severe pneumonia in children; clinical monitoring; comprehensive nursing
Reference

Dermatology

皮肤

分类：7. Dermatology 皮肤
746

Prevalence of pediatric dermatological disorders of the COVID-19 pandemic in China

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Background: Epidemiological studies of pediatric dermatological disorders are rather rare. The aim of this study was to determine the spectrum of pediatric dermatological disorders before and during the COVID-19 pandemic in China.
Methods: This retrospective study encompasses consecutive patients attending a number of dermatological outpatient clinics in Beijing Children's Hospital from 1 January 2019 and 31 December 2020. Diagnosis was mainly based on clinical findings, but supplemented by further investigations when needed.
Results: The total number of patients was 298572, including 184301 cases with 134276 newly pathological conditions reported in 2019 and 114271 cases with 84155 newly pathological conditions reported in 2020 respectively. The mean age was 4.42 years in 2019 with a M/F sex ratio of 1.17:1and 4.65 years in 2020 with a M/F sex ratio of 1.13:1. The proportion of school-age children is the highest. The geographical distribution includes 32 provinces, cities and autonomous regions in China. During the COVID-19 pandemic in 2020, Atopic Dermatitis and other Types of Dermatitis constituted the major group of disorders (38.79%), followed by Infections(15.31%), Urticaria, Erythemas and Drug Reactions(8.96%), Parasitic Skin Infestations and Sting Reactions(7.23%). The top five new-onset diagnosed dermatological disorders in descending order of incidence were Atopic dermatitis (N: 24950, 28.63%), Urticaria (N: 7206, 8.56%), Papular urticaria (N: 5898, 7.01%), Melanocytic naevi (N: 4098, 4.87%) and Acne (N: 3313, 3.94%). Moreover, pediatric tele dermatology may be used to increase timely access and enhance practice efficiency during the epidemic.
Conclusions: This study provides useful information about the prevalence of pediatric dermatological disorders during the COVID-19 pandemic in China.

关键字 Dermatological Disorders, Pediatric, the COVID-19 Pandemic, China

分类：7. Dermatology 皮肤
770

Low dose propranolol in the treatment of parotid hemangioma in premature infants

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A case of 30 weeks of gestation, birth weight 1780g infant with parotid hemangioma at 2 weeks after birth. A decrease in surface telangiectasia was observed at the dose of 0.25 mg/kg per day on the 3rd day after administration, and a disappearance of surface telangiectasia was observed at the dose of 0.5 mg/kg per day on the 6th day after administration, the tumor had shrunk significantly.

关键字 infantile hemangioma, propranolol, pediatric dermatology

分类：7. Dermatology 皮肤
804

Polarized and ultraviolet dermoscopy of tinea of scalp and eyebrows and review of published literature

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Abstract
Objectives. To investigate the epidemiology, clinical manifestation, treatment, and prognosis of tinea of eyebrows, and to report a case of tinea of scalp and eyebrows caused by Microsporum canis and ultraviolet dermoscopic characteristics.
Methods. Clinical and laboratory findings of the case were studied, and cases of tinea of eyebrows were collected and analyzed.
Results. A 5-year-old boy presented with scalp and face lesions. An annular erythema with scaling and hair loss was observed on the right parietal scalp, and multiple annular scaling patches involving the eyebrows were observed on the face. Direct microscopic examination of the lesional hairs and face lesions revealed numerous ectothrix spores and fungal hyphae, respectively. The isolates grown in culture were identified as M. canis. Comma hairs were observed on the scalp and eyebrows under polarized dermoscopy. The fluorescent hairs on the eyebrows were markedly shorter than those on the scalp under ultraviolet dermoscopy, indicating that hairs break at a lower level on the eyebrows. Reviewing the English literature, only eight other cases of tinea of eyebrows have been reported worldwide.
Conclusions. We speculate that eyebrows are thinner than hairs on the scalp and easier to be broken by M. canis. This finding will enhance our knowledge about pathogenesis of dermatophytosis.

关键字 Microsporum canis; tinea capitis; eyebrows; ultraviolet dermoscopy; itraconazole

分类：7. Dermatology 皮肤
838

A Case of congenital ichthyosiform erythroderma accompanied with atopic dermatitis

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Background: Congenital ichthyosiform erythroderma belongs to autosomal recessive congenital ichthyosis, which is characterized by fine, whitish scales on a background of erythematous skin. It is reportedly caused by mutations in ABCA12, ALOX12B, ALOXE3, CERS3, CYP4F22, NIPAL4, PNPLA1 and TGM1 and other unidentified genes. Here we conduct gene mutation detection and analysis in an 1-year-old male infant with erythema, scales and itching. **Method:** The clinical data of the patient was collected. The DNA from the peripheral blood of patient and his parents was extracted and sequenced with the congenital ichthyosis multi- gene chip by next generation sequencing, and Sanger sequencing was used to verify the selected variants. **Results:** The homozygous mutation c.433C>T, p.Arg145Ter in the NIPAL4 gene was found in the patient, and both parents were heterozygous carriers. **Conclusion:** Homozygous missense mutations (c.433C>T, p.Arg145Ter) in NIPAL4 might lead to a congenital ichthyosiform erythroderma phenotype accompanied by atopic dermatitis.

关键字 Congenital ichthyosiform erythroderma, Atopic dermatitis, NIPAL4 gene, homozygous mutation

分类：7. Dermatology 皮肤
839

Novel ABCA12 compound heterozygous mutations identified in a case of congenital ichthyosiform erythroderma

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Background: Mutations in ABCA12 have been described in autosomal recessive congenital ichthyoses (ARCI) including harlequin ichthyosis (HI), congenital ichthyosiform erythroderma (CIE) and lamellar ichthyosis (LI). Here we conduct gene mutation detection and analysis in a patient of CIE with erythema and scales. Method: The clinical data of the patient was collected. The DNA from the peripheral blood of patient and his parents was extracted and sequenced with the congenital ichthyosis multi- gene chip by next generation sequencing, and Sanger sequencing was used to verify the selected variants. Results: The novel compound heterozygous mutations (c.7402C＞T, c.4978-5T＞G) in ABCA12 gene were found in the patient which came from his parents separately. Conclusion: Compound heterozygous mutations (c.7402C＞T, c.4978-5T＞G) in ABCA12 might lead to this patient's phenotpye of congenital ichthyosiform erythroderma.

关键字 Congenital ichthyosiform erythroderma, ABCA12 gene, compound heterozygous mutations

分类：7. Dermatology 皮肤
932

Propranolol inhibits the angiogenic capacity of hemangioma endothelia via blocking β-adrenoceptor in mast cell

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BACKGROUND: Propranolol, a non-selective blocker of the β-adrenoceptor (AR), is a first-line treatment for infantile hemangioma (IH). Mast cells have been implicated in the pathophysiology of propranolol-treated hemangioma. However, the function of mast cells remains unclear.
METHODS: HMC-1s (Human mast cell line) having been treated with propranolol for 24 h were centrifuged, washed with PBS twice, and maintained in cell culture medium for another 24 h. The supernatants with propranolol which were named as propranololtreated HMC-1s supernatants were obtained. The expression of cytokines and mediators was examined among HMC-1s dealt with propranolol. HemECs (hemangioma endothelial cells) were co-cultured with propranolol-treated HMC-1s supernatants, and their proliferation and apoptosis were investigated. The autophagic-related protein was examined in HemECs using immunoblot.
RESULTS: In propranolol-treated HMC-1s, the expressions of ADRB1(β1-AR) and ADRB2 (β2-AR) were reduced by 70% and 60%, respectively, and that of cytokines and mediators were reduced. The proliferation was decreased, but apoptosis and autophagy were induced in HemECs treated with propranolol-treated HMC-1s supernatants. However, propranolol can work well in shRNAADRB1 or shRNA-ADRB2 transfected HMC-1s.
CONCLUSIONS: Propranolol inhibit the proliferation of HemECs and promote their apoptosis and autophagy through acting on both β1 and β2 adrenoceptor in mast cell.

关键字 propranolol; infantile hemangioma; mast cell; mechanism; angiogenic capacity

分类：7. Dermatology 皮肤
941

A 6-year-old girl of hemangioma with hearing loss in right ear

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3. 首都

A 6-year-old girl presented to our clinic due to hemangioma on her right face since birth with hearing loss in her right ear. 2 days before she presented to dental clinic due to enamel hypoplasia and caries. Personal history: 37 weeks gestation with cesarean section, the smaller of twins, birth weight 2520g, at 24 weeks of pregnancy found that the right extracerebellar space increased, birth weight 2520g. Examination showed right side of the face, forehead, and nasal root are telangiectasia. Erythema is visible on the right upper lip, right maxillary gingiva and right upper jaw. The right side of the face is slightly larger than the opposite side. On enhanced CT, there were localized bony defects at the base of the middle cranial fossa on the right side of the skull. The other part of skull was intact, the brain structure was normal. Ultrasound showed that the right part of the teeth had a little thick periodontal membrane, the gingival blood supply increased, the UCG did not show obvious abnormality, the hearing results showed severe conductive deafness in the right ear and no obvious abnormality in the fundus of both eyes.

关键字 infantile hemangioma, hearing loss, enamel hypoplasia, caries

分类：7. Dermatology 皮肤
1126

Sparse hair with delayed closure of fontanelle for 1.5 years

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Objective: To detect gene mutations and make a diagnosis in a patient with alopecia and large skull defect.
Methods: Clinical data were collected from the proband, and genomic DNA was extracted from peripheral blood samples from the proband and her parents. Exome sequencing was performed in the proband by using a gene panel targeting hereditary skin diseases to identify mutation sites, and then the candidate mutation site was verified by PCR and Sanger sequencing among her family members. Results of peripheral blood smear examination and other auxiliary examinations were collected from the proband and his parents and analyzed.
Results: The proband presented with alopecia, hypertelorism and large skull defect, wide nasal bridge, broad and depressed nasal tip. Exome sequencing revealed a heterozygous mutation c.1016dupC in exon 4 of the ALX4 gene encoding transcription factor in the peripheral blood genomic DNA of the proband, resulting in a frameshift mutation p.G340Wfs*104 in the amino acid sequence. This mutation was de novo and wasn’t detected in her parents.
Conclusion: The diagnosis of frontonasal dysplasia-2 was made in the proband based on the presentation of alopecia, hypertelorism and large skull defect, wide nasal bridge, broad and depressed nasal tip, as well as the heterozygous mutation in the ALX4 gene.This is the first case of frontonasal dysplasia-2 caused by ALX4 in china.

关键字 Alopecia,Large skull defect,DNA mutational analysis,ALX4,frontonasal dysplasia-2

分类：7. Dermatology 皮肤
1285

A case of Rothmund-Thomson syndrome type II accompanying with Hodgkin lymphoma and Phenylketonuria

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Objective：To illustrate the diagnosis, treatment and prognosis of a rare case.
Methods: Basing on the medical history, laboratory tests, imaging examinations, biopsy and genetic testing, the final diagnosis was made. Following up and recording the change of illness.
Results: A 14-year-old girl with a 5-month history of multiple cutaneous nodules on the scalp and buttock. Meanwhile, similar lesions appeared on the forehead and perioral region, and the ulcers developed on the primary nodular lesions. The topical antibiotic ointment was ineffective. Twenty days before admission, she began with intermittent fever, and the highest temperature was 39.4 ℃. The patient presented with poikiloderma of face and hands, and hyperpigmentation of trunk and extremities. The patient was diagnosed with phenylketonuria (PKU) when she was 20 months old.

The bone marrow examination showed active proliferation with no atypical lymphocytes. Positron Emission Tomography-Computed Tomography (PET-CT) scan revealed multiple nodules in both lungs and liver, and enlarged lymph nodules located in bilateral neck, hilum of lung, mediastinum, mesentery, retroperitoneum, and porta hepatis, where we could find the increased concentrations of radioactive material. The histopathological findings were in accordance with Hodgkin lymphoma. The results of whole-exome sequencing revealed the mutations of PAH and RECQL4 genes. The final diagnosis was Rothmund-Thomson syndrome (RTS) type II accompanied with HL and PKU.

The patient has been treated with “four courses of ABVD (Adriamycin, Bleomycin, Vincristine, Dacarbazine) regimen”, “two courses of Sintilimab (Anti-PD-1 Antibody) combined with Cisplatin and Gemcitabine” and “eight courses of Brentuximab (Anti-CD30 Antibody) combined with Etoposide and Epirubicin”in succession. The original skin ulcers on the scalp, face and buttock have been healed, and the results of CT revealed that the conditions of organs other than skin have improved significantly.
Conclusion: RTS is a rare disease associated with gene mutations. Early diagnosis and long term follow-up are very important owing to increased risk of cancers. The timely and effective treatment for cancers would be crucial to the prognosis of patients.

关键字 Rothmund-Thomson syndrome; Hodgkin lymphoma; Phenylketonuria; RECQL4

分类：7. Dermatology 皮肤
1340

A novel ABHD5 gene mutation causes Chanarin-Dorfman syndrome in two siblings in a Chinese pedigree

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Background：Chanarin-Dorfman syndrome (CDS, MIM 275630) is a rare autosomal recessive disorder characterized by neutral lipid accumulation in numerous organs and tissues. Here, we report two siblings with CDS caused by a compound heterozygotic mutation in the ABHD5 gene.
Method：Clinical and related laboratory examination datas of the patients were collected. Meanwhile, peripheral blood of the proband, her family members were collected, whole exon sequencing analysis was performed on the proband, and Sanger verification for her family members.
Results：The proband was a 4-month-old girl, presenting with localized dry and scaly skin on her face, trunk and limbs. Her elder brother, a 5-year-old boy, was diagnosed with ichthyosis at birth. Both of them had granulocyte lipid vacuoles in peripheral blood smears, accompanied by hepatomegaly, fatty liver and abnormal liver function.Genetic testing revealed a novel nonsense mutation c.56G>A (p.Trp19Ter) in exon 2 of the ABHD5 gene combined with a frameshift mutation c.347delG (p.Ser116IlefsTer27) in exon 3.
Conclusions：Ichthyosis skin lesions and fatty liver combined with peripheral smear examination can help clinicians make the diagnosis of CDS as soon as possible.

关键字 ichthyosiform erythroderma；hepatomegaly；ABHD5 gene mutation

分类：7. Dermatology 皮肤
1401

Serum vitamin E at early gestation and risk of atopic dermatitis on infants: a prospective birth cohort in China

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Background: Maternal nutrition status was posed to link with developing allergy on offspring. The results about maternal vitamin E and childhood atopic dermatitis were inconclusive. We aim to assess the relationship between maternal vitamin E level in early gestation and infant AD and explore its effect on newborn skin barrier.
Methods: Pregnant women (n=410) from MKFOAD (NCT02889081) were recruited at 12-14 weeks of gestation in Shanghai, China. Serum vitamin E concentrations (alpha tocopherol) were examined by liquid chromatography–tandem mass spectrometry. We collected maternal social demographic, parental allergic history through questionnaire and infant birth information by medical record. We examined transepidermal water loss (TEWL) at forehead and cheek at birth and 42 days. Infant AD was diagnosed according to Williams' criteria. Multivariable logistic regression was used to evaluate association of maternal vitamin E level with infant AD. Linear regression was tested on the relationship of maternal vitamin E with infant TEWL at birth or 42 day.
Results: In total, 112 (27.3%) infants developed AD before 1 year, with more male infants affected (p =0.004). Higher maternal vitamin E levels were associated with a reduced risk of AD (aOR 0.92, 95% CI 0.85-0.99) and lower TEWL value on forehead at birth (β=-0.026, p=0.011). Infant born to mother with the highest tertile of vitamin E had lower risk of AD by 53% (aOR 0.47, 95% CI 0.26-0.86) compared to lowest tertile.
Conclusions: We provide the first evidence that higher maternal vitamin E concentration during early gestation is associated with reduced early-onset infant AD. Our findings support that maintaining appropriate vitamin E level during pregnancy might be important to prevent AD risk on infant.

关键字 vitamin E; pregnancy; birth cohort; atopic dermatitis; infant; skin barrier

分类：7. Dermatology 皮肤
1415

A case of primary cutaneous amyloidosis misdiagnosed as vitiligo

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Primary cutaneous amyloidosis (PCA) is a chronic pruritic skin disease with characteristic amyloid deposits in the papillary dermis. The main forms of PCA include macular amyloidosis and lichen amyloidosis. Other uncommon types include poikiloderma-like amyloidosis, amyloidosis cutis dyschromica, bullous amyloidosis, and ano-sacral amyloidosis. We herein report a case of PCA with uncommon manifestation misdiagnosed as vitiligo initially. Through biopsy and histopathological observation, the boy was diagnosed as primary cutaneous amyloidosis (PCA). This case differs from the common subtypes of PCA, and most other cases reported in literature due to presence of hypopigmented macules as the only cutaneous finding.

关键字 primary cutaneous amyloidosis；vitiligo；hypopigmented

分类：7. Dermatology 皮肤
1431

A boy with symmetrical hyperpigmented patches on the buttocks

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Pityriasis versicolor is a superficial fungal infection of the skin. Its implicated pathogens are Malassezia, a lipophilic dimorphic fungus. Despite the fact that it belongs to the normal skin flora, conversion from the yeast to the pathogenic hyphal form is essential for the development of disease. In this report, we report a case of a Chinese boy with symmetrical, well-demarcated and large hyperpigmented patches without scaling on the buttocks without other abnormity, and the boy was suspected as exogenous pigmentationinitially. Through direct microscopy with 10% potassium hydroxide, the boy was diagnosed as pityriasis versicolor. And the lesions were completely remissive with topical terbinafine treatment. This case differs from the common anatomical distribution of pityriasis versicolor. The reasons may be sweating excessively and sedentary study. Therefore, pityriasis versicolor should be considered when present hyperpigmented patches in the hyperhidrotic areas except the common anatomical distribution.

关键字 buttock, hyperpigmented, pityriasis versicolor

Disaster Preparedness

灾害管理

Category: 8. Disaster Preparedness 灾害管理
1348

The estimated age-group specific influenza vaccine coverage rates in Hong Kong and the impact of the school outreach vaccination program

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Abstract Content Seasonal influenza strikes annually causing millions to fall sick and several hundred thousand to die globally. Hence, universal vaccination is a public health aim to control influenza. The Hong Kong Government started to introduce the School Outreach Vaccination (SOV) program in 2018 to increase vaccination rates in children. This study has three aims: (1) to demonstrate the effect of SOV on the vaccination rate between 2019 and 2020, (2) to look at the impact SOV program on influenza hospital admission, (3) and to estimate vaccination rates in the total population of Hong Kong.

Methods 2376 students were recruited randomly for this study, which used a questionnaire-based tool. The first questionnaire was sent out in 2019 to measure influenza vaccination coverage and influenza-like symptoms of the students. In 2020, further information surrounding household members and their vaccination rate was included in the data surrounding the student vaccination rate. The influenza vaccination rates for specific age groups who are in the Government universal vaccination program over the three years (2017/18, 2018/19, and 2019/20) were retrieved from the website of the Centre for Health Protection (CHP) of the Department of Health (DH) and compared with the estimated influenza vaccination rates [1]. Influenza hospital admission data for children aged <12 years old were extracted from the HA electronic database. Using the information about household members and their ages, the vaccination coverage for the total Hong Kong population across different age groups can be estimated using the census data.

Results There was no significant difference in the influenza vaccination rate of primary school children between the two survey years, 69.2% versus 69.5% (p=0.8428) [2]. The SOV program significantly increased vaccination coverage rates with a 1 % increase associated with a reduction of 4.3 influenza-related hospital admissions of school-aged children. The estimation of vaccine coverage rates among the under 5-year-olds (48.5%), primary school children (69.3%), and over 65-year-olds (45.7%).

Conclusion The SOV program significantly improved the primary school students' vaccination rate and therefore substantially reduced the number of influenza-related hospital admissions. Extension of the SOV program should be considered in secondary schools to increase the coverage rates in adolescents. The questionnaire survey may inform the government how to achieve universal vaccination for specific age groups. Considering the need for rapid implementation of universal vaccination to curb the COVID-19 pandemic, this current experience of influenza vaccine SOV could be expanded to cover COVID-19 vaccine administration for school children.

Key words Influenza, Vaccine, Schools, Public Health, Public Health Policy, Vaccination Program

Reference [1] Centre for Health Protection. Department of Health - Statistics on Vaccination Programmes in the Past 3 years. 2021[2] Lau YL, Wong WHS, Hattangdi-Haridas SR, Chow CB. Evaluating impact of school outreach vaccination programme in Hong Kong influenza season 2018 - 2019. Human Vaccines & Immunotherapeutics 2020; 16:823-6.

Category: 8. Disaster Preparedness 灾害管理
1355

Adolescents' attitudes to the COVID-19 Vaccination

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Abstract Content Vaccines against COVID-19 are now available for adolescents in Hong Kong but vaccine hesitancy is a major barrier to herd immunity. It is influenced by three main factors: confidence (lack of trust in the safety and efficacy of a vaccine), complacency (low perception of disease risk), and convenience (access including availability and affordability) [1]. Studies directly exploring the willingness of adolescents to receive the COVID-19 vaccine are lacking, therefore, this survey study explores Hong Kong adolescents' attitudes towards the COVID-19 vaccination to identify the factors that could improve vaccine uptake.

Methods 2609 adolescents from across Hong Kong completed an online survey between May and June 2021 containing a series of predominantly yes-no questions or multiple-choice questions and primarily focused on the child's intent to vaccinate and the reasons for their choice. Only those children within the adolescent age range (12 to 18 years) were included.

Results 1007 (39%) adolescents intended to take the COVID-19 vaccination and significant factors for this decision include: having at least one parent vaccinated, knowing somebody diagnosed with COVID-19, and receiving the influenza vaccine. Adolescent's major concerns either surrounded the safety and efficacy of the vaccine or the risk of themselves or their family being infected. Although previously being quarantined and completing compulsory testing were not statistically significant on analysis, we predict that this is due to the small population size of these subgroups and suspect that larger sample size may show a significant association.

Conclusion This study has proved that even in adolescents the vaccine hesitancy model is prominent with adolescents' intentions highly related to confidence in the vaccine and perception of disease risk. Future interventions should target these specific concerns to ensure adolescents are well educated to overcome vaccine hesitancy.

Key words COVID-19, Vaccine, Public Health, Paediatrics, Attitudes

Reference [1] Sallam M. COVID-19 Vaccine Hesitancy Worldwide: A Concise Systematic Review of Vaccine Acceptance Rates. Vaccines. 2021;9:160.

Psychology Mental

Health

心理

Category: 22. Psychology Mental Health 心理
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Prevalence and risk factors for children psychological health during the COVID-19 pandemic: A cross-sectional study

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Abstract Content Studies reported the negative emotions were existed during pandemics around the world owing to restricted daily activities. We therefore performed this study to assess the prevalence and risk factors related to psychological health in children during the COVID-19 pandemic.

Methods A total of 1,124 primary school children aged from 6.0-10.0 years were recruited throughout online survey forms. The psychological health were assessed using the Strengths and Difficulties Questionnaire (SDQ), and the domains including prosocial behavior, hyperactivity-inattention, emotional symptoms, conduct problems, and peer relationship. Multiple logistic regression were applied to identify potential risk factors for psychological health, and odds ratio (OR) with 95% confidence interval (CI) were used as effect estimate. Stratified analyses according to gender were also reported.

Results Of 1,124 recruited children, a total of 668 children presented abnormal psychological health, and the number of abnormal for prosocial behavior, hyperactivity-inattention, emotional symptoms, conduct problems, and peer relationship were 86, 169, 111, 132, and 323 children, respectively. The risk factor for abnormal psychological health in overall cohort (P=0.035) and male cohort (P=0.006) was times of fruit intake per week, while number of interest classes was associated with an increased risk of abnormal psychological health in female (P<0.050). Moreover, the risk factor for abnormal prosocial behavior was the duration of exercising (P=0.020) in overall cohort, while the risk factors included family formation (P=0.044), education level of mother (P=0.007), and time for mother with children on workday (P=0.032) for male cohort. Education level of father was associated with an increased risk of abnormal hyperactivity-inattention in overall cohort (P=0.039) and female cohort (P=0.017), while duration of sleeps of children could induce abnormal hyperactivity-inattention in overall cohort (P=0.012) and male cohort (P=0.032). The risk factors for abnormal emotional symptoms included single-parent family (P=0.007), education level of mother (P=0.049), and the number of interest classes (P=0.020). Furthermore, the number of interest classes was associated with an increased risk of abnormal emotional symptoms in male cohort (P<0.050), while the risk factors for abnormal emotional symptoms in female cohort contained family formation (P=0.012), and father's education level (P=0.028). We noted the number of interest classes was associated with an increased risk of abnormal conduct problems in female cohort (P=0.017). Mother's education level could affect the risk of abnormal peer relationship in overall cohort (P=0.032) and male cohort (P=0.046), while dairy intake per day could affect the risk of abnormal peer relationship in male cohort (P=0.038).

Conclusion This study reported comprehensive risk factors for psychological health and domains of prosocial behavior, hyperactivity-inattention, emotional symptoms, conduct problems, and peer relationship in children during COVID-

19 pandemic. Further prospective study should be performed to verify the results of this study.

Key words risk factors,children psychological health,COVID-19
Reference 1. World Health Organization Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance, 28 January 2020. World Health Organization; (2020). https://apps.who.int/iris/handle/10665/330893.2. WHO Director-General’s opening remarks at the media briefing on COVID-19 - 11 March 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19%2D%2D-11-march-2020. 3. Sprang G, Silman M. Posttraumatic stress disorder in parents and youth after health-related disasters. Disaster Med Public Health Prep 2013;7:105-10. 4. Xie X, Xue Q, Zhou Y, et al. Mental Health Status Among Children in Home Confinement During the Coronavirus Disease 2019 Outbreak in Hubei Province, China. JAMA Pediatr 2020; 174:898-900.5. Zhou SJ, Zhang LG, Wang LL, et al. Prevalence and socio‐demographic correlates of psychological health problems in Chinese adolescents during the outbreak of COVID‐19. Eur Child Adolesc Psychiatry 2020;29:749‐758.6. Jiao WY, Wang LN, Liu J, et al. Behavioral and emotional disorders in children during the COVID‐19 epidemic. J Pediatr 2020;221:264‐266.7. Saurabh K, Ranjan S. Compliance and psychological impact of quarantine in children and adolescents due to Covid‐19 pandemic. Indian J Pediatr 2020;87:532‐536.8. Chen IH, Chen CY, Pakpour AH, et al. Internet-Related Behaviors and Psychological Distress Among Schoolchildren During COVID-19 School Suspension. J Am Acad Child Adolesc Psychiatry 2020;59:1099-1102.e1.9. Duan L, Shao X, Wang Y, et al. An investigation of mental health status of children and adolescents in China during the outbreak of COVID‐19. J Affect Disord 2020;275:112‐118.10. Larsen B, Luna B. Larsen B, Luna B. Adolescence as a neurobiological critical period for the development of higher-order cognition. Neurosci Biobehav Rev 2018;94:179-195.11. Goodman R. The strengths and difficulties questionnaire: a research note. J Child Psychol Psychiatry 1997;38:581-586.12. Bilginer Ç, Yildirim S, Çekin Yilmaz B, et al. Changes in adolescent mental health during the covid pandemic. Minerva Pediatr (Torino). 2021 Apr 23. doi: 10.23736/S2724-5276.21.06178-4. 13. Mautong H, Gallardo-Rumbea JA, Alvarado-Villa GE, et al. Assessment of depression, anxiety and stress levels in the Ecuadorian general population during social isolation due to the COVID-19 outbreak: a cross-sectional study. BMC Psychiatry 2021;21:212.14. Thomas MM, Gugusheff J, Baldwin HJ, et al. Healthy Lifestyle Behaviours Are Associated with Children's Psychological Health: A Cross-Sectional Study. Int J Environ Res Public Health 2020;17:7509. 15. O'Neil A, Quirk SE, Housden S, et al. Relationship between diet and mental health in children and adolescents: a systematic review. Am J Public Health 2014;104:e31-42. 16. Huang N, Qiu S, Alizadeh A, et al. How Incivility and Academic Stress Influence Psychological Health Among College Students: The Moderating Role of Gratitude. Int J Environ Res Public Health 2020;17:3237. 17. Okuyama J, Seto S, Fukuda Y, Funakoshi S, Amae S, Onobe J, Izumi S, Ito K, Imamura F. Mental Health and Physical Activity among Children and Adolescents during the COVID-19 Pandemic. Tohoku J Exp Med 2021;253:203-215.18. Bot M, de Leeuw den Bouter BJ, Adriaanse MC. Prevalence of psychosocial problems in Dutch children aged 8-12 years and its association with risk factors and quality of life. Epidemiol Psychiatr Sci 2011;20:357-65. 19. Carpena MX, Munhoz TN, Xavier MO, et al. The Role of Sleep Duration and Sleep Problems During Childhood in the Development of ADHD in Adolescence: Findings From a Population-Based Birth Cohort. J Atten Disord 2020;24:590-600.20. Kuruczova D, Klanova J, Jarkovsky J, et al. Socioeconomic characteristics, family structure and trajectories of children's psychosocial problems

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分类：22. Psychology Mental Health 心理
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Study on the family function of school-aged children during the COVID-19 quarantine

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[Abstract]:Objective:Investigate the family functions status of school-age children during the period of COVID-19 quarantine, and provide relevant intervention strategies for similar public health events in the future.Method:A primary school in a certain district of Shanghai, China was selected for cluster sampling, giving student’s parents the general questionnaire and family intimacy & adaptability surveys. In order to investigate the basic conditions and family functions of children and families isolated at home during the COVID-19 pandemic for the past 6 months..Results: The family adaptability and family intimacy of school-age children were 48.31±8.43 and 71.62±10.33 respectively during the quarantine period.Among them, whether the only child, left-behind children, family per capital income and parents' educational level have statistical significance on children's family adaptability (P<0.05).Left-behind children, family type, family per capital income and parents' educational level had statistically significant effects on the scores of family intimacy (P<0.05).Conclusion: During the COVID-19 outbreak, school-age children’s family functions will change, and family environmental factors should be considered comprehensively, especially for vulnerable groups.

关键字 COVID-19;family function;school-aged children

分类：22. Psychology Mental Health 心理
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The Research on Intervention Effects of Executive Function Training on Children with ADHD

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Background: Executive function defect is considered as one of the key defects in children with attention deficit hyperactivity disorder (ADHD). Currently, executive function training for ADHD children is mainly focused on working memory training (WMT), while executive function training, with a wide range of executive function facets being trained, has not been paid more attention.
Purpose: This study was aimed to explore the effect of executive function group training (EFGT) on executive function and clinical manifestations of ADHD children. Meanwhile, the effect of working memory training was compared.
Patients and Methods: Fifty-three ADHD children were randomly divided into EFGT group (study group) and WMT group (control group). In study group, group therapy was conducted for eight times once a week, which contained a wide range of executive function training, including response inhibition, working memory, time management, emotional recognize, emotional regulation, and so on. At the same time, computerized working memory training was conducted for children in control group. Then, the executive function and clinical manifestations in both two groups were assessed before and after intervention, SNAP-IV, WISC-IV, Stroop color-word associated test and WCST were used. The effect of intervention in both two groups was compared before and after intervention. Meanwhile, the intervention effect of two groups were compared.
Results: The expulsion rate of study group was 12.5% after 8 weeks, which showed no significant difference with control group ($\chi 2=0.416$, $P=0.421$). In study group, it was found that the number of corrections in first subtest of SCWT significantly increased after intervention ($t=-2.82$, $P < 0.05$), and the ODD subscale in the SNAP-IV significantly decreased after intervention ($t=3.12$, $P<0.05$). ANCOVA showed the categories completed, conceptual level and perseverative responses in WCST and decoding subtest were significantly higher than those in control group than study group ($F=4.120-18.020$, $P<0.05$). The completed time of test B in Stroop in control group was significantly lower than it in control group ($F=5.731$, $P=0.021$).
Conclusion: The results suggest EFGT has positive effects on improving executive function and clinical manifestations of ADHD children. Although children with ADHD benefits more working memory training in clinical manifestation. EFGT can specially improve their oppositional behavior in some ways.

关键字 ADHD; Executive function training; Group training; Working memory training

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Research on Social Decision-making Behaviors of Adolescent Depression Patients

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Background: Depressive disorder is one of the common mental disorders in adolescence, which has a great impact on the social function of adolescents. At present, the research on social function is relatively limited. Recent research focuses on social decision-making behavior, and some related researches mainly study social decision-making behavior in social interaction scenarios based on game theory. In this research paradigm, two participants allocate a sum of money. One of them, as a proposer, proposes an allocation scheme to the other respondent, and the respondent can accept or reject the scheme. If accepted, it will be allocated according to the proposer's plan; if rejected, neither will get money. There were differences in previous research results, some of the studies suggested that there was significant difference between depression group and control group, while others showed that there was no significant difference between the two groups. In addition there is no specific research to explore the characteristics of teenagers' social decision-making behavior.
Purpose: To explore the abnormal social decision-making behavior of adolescent depression patients, and then reflect their social function.
Method: 49 patients with adolescent depression and 25 healthy adolescents were included in this study. The differences of acceptance rate and reaction time of adolescent depression patients and healthy adolescents were investigated by Ultimatum Game. Hamilton Depression Scale-17 (HAMD-17), The Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder (GAD-7), Childhood Trauma Questionnaire (CTQ)and Adolescent Self -rating Life Events Check-list (ASLEC) were included to analyze the relationship between related indicators and social decision-making behavior.
Result: Acceptance rate: there was no significant difference between the adolescent depression group and the normal control group ($P > 0.05$), but the main effect of fairness ($F = 201.760$, $P < 0.001$) and the interaction between fairness and proposer category ($F = 8.791$, $P = 0.004$) had statistical significance on the acceptance rate. Reaction time: there was no significant difference between the two groups. However, the main effect of the fairness of the scheme is statistically significant ($F=42.755$, $P<0.001$,partial $\eta 2=0.373$),and the main effect of Proposer is also statistically significant ($F=5.333$,$P=0.024$,partial $\eta 2=0.069$), and the interaction between fairness and proposer was statistically significant ($F=8.946$,$P=0.004$,partial $\eta 2=0.111$).
Conclusions: This study found that there was no significant difference in social decision-making behavior between adolescent depression group and normal control group. The similar cognition of the fairness of the scheme may be an important reason for the no significant difference in the acceptance rate of the scheme between the two groups. In the face of unfair proposals, adolescent depression patients are more likely to choose to accept than normal people. This may be because the sensitivity of patients with adolescent depression is improved,and they instinctively put the other party's possible response into consideration. In addition,this study found that the acceptance rate of the two groups for unfair distribution scheme is lower than that of fair scheme,which may be because unfair scheme will cause more negative emotions,and then affect the acceptance rate.Finally,this study found that

adolescents with depression have a clear distinction between human and computer,which may be related to the fact that they are more immersed in social interaction.

关键字 Adolescent depressive disorder;ultimatum game theory; social decision making behavior

分类：22. Psychology Mental Health 心理

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A Nationwide Screening and Survey of ADHD in Primary Schools of Urban Areas in China

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8. 浙江大学医学院附属儿童医院
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13. 四川大学华西第二医院

Objective: Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder in childhood. The objective of this study was to investigate the positive rate of screening and current diagnostic and treatment statuses of ADHD among school-age children in urban areas of China.

Methods: This cross-sectional study included 308 classes in 52 primary schools in 13 cities of 7 major geographical regions in China through stratified cluster random sampling. In each primary school, one class was randomly selected per grade for screening, and the parents and teachers of the selected school-age children were asked to fill out the Chinese version of the SNAP-IV Rating Scale separately. The positive rates of screening from SNAP-IV scale-parent and teacher forms were calculated, and screening results in parents and teachers were compared. Meanwhile, the parents were also surveyed to investigate the current diagnostic and treatment statuses of ADHD among school-age children.

Result: A total of 12,376 school-age children were screened (53.1% boys, with median age of 9 years), and 12,376 parents (73.2% mothers) and 302 teachers (95.7% females) were investigated. The findings were as follows. (1) In China, the positive rates of screening by parents and teachers were 4.5% and 6.0%, respectively. In North and Central China, the positive rates of screening by parents and teachers were similar, with no statistically significant differences (P>0.05), while in other geographical regions, the positive rates of screening were higher for teachers compared with parents, and the differences were statistically significant (P<0.05). (2) Among the children who have been screened as potential ADHD cases by parents, only 26.6% had visited a doctor previously because of ADHD symptoms, versus only 25.3% in those screened by teachers. Among the 12,376 school-age children, only 14% had visited a doctor before because of ADHD symptoms, of whom 7.7%, 3.4% and 2.9% had visited children's, general and specialized psychiatric (psychological) hospitals, respectively. The main problems encountered by parents when taking their children to see a doctor were that they could not find a specialized ADHD clinics (39.4%), they could not fully communicate with the doctors (37.2%), they could not make an appointment (30.9%), and waiting time was too long (30.7%). (3) Of the school-age children screened, 1.4% were once diagnosed with ADHD, and 1.5% were current ADHD cases. Of the children previously diagnosed or current ADHD, 49.8% received no ADHD treatment in the past 12 months, 24.7% received pharmaceutical treatment, 12.8% received non-pharmaceutical treatment, and 12.8% received combined treatment.

Conclusion: Many children with ADHD in China have not seen a doctor for proper diagnosis. ADHD children in China obviously encounter many difficulties in visiting a doctor, and suffer from inadequate diagnosis and treatment, especially inadequate pharmaceutical treatment. Improving parents' and teachers' awareness of ADHD, establishing scientific specialized ADHD clinics and training more doctors specialized in ADHD would be much helpful to achieve early detection, diagnosis and intervention of ADHD, making children obtain sufficient medical resources and good doctor-patient communication, further improving patient prognosis.

关键字 Attention deficit hyperactivity disorder, school-age children, screening, current statuses of diagnosis and treatment

分类：22. Psychology Mental Health 心理
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Qualitative Study on Psychological Experience and Transitional Care Needs of Parents of Children with Limb Fracture

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Objective: To understand the psychological experience and nursing needs of parents of children with limb fractures during hospitalization, analyze the causes and propose coping strategies. Methods: With convenience sampling method, father or mother of the children with limb fractures who were hospitalized in our department from April to June 2021 were selected as research subjects to be conducted semi-structured interviews. Before the interview, We the purpose of the study to the subjects was introduced, the informed consent of the subjects was obtained,the whole process of the interview was recorded and the interview notes and memos were made. Interview skills were paid attention to use to create a relaxed atmosphere.The interview time was approximately 30~60 minutes.The core content of the interview outline were: ①what do you feel about your child being hospitalized? ②Why do you feel like this? ③Do you want to be provided transitional care after discharge? If so, in what areas do you want to be guided or cared? What kind of form do you want to be given service to? Tranthe recording as a document within 24 hours of the interview.The phenomenological data 7-step analysis method by Colaizzi was adopted to organize, code, analysis and summarize the collected data. Results: 14 parents were anxious about the child ' s pain, 12 parents were worried about the prognosis of the child ' s fracture, 2 parents were guilty or blamed for the child ' s fracture, and 4 parents were burdened with stress, 7 parents of school-age children were worried about affecting their children's study, all parents were worried about affecting their children's lives, 2 parents felt the financial burden was heavier, most of the parents interviewed needed transitional care, the interview content were mainly functional exercise guidance,gypsum care,traction nursing, prevention of secondary fractures, prevention of complications, nutrition guidance, etc. One case wanted family visit, most of them wanted telephone visit, two cases prefered WeChat access. Conclusion: There were obvious psychological problems in the parents of children with fractures during hospitalization, and there was a certain need for transitional care. During hospitalization, it was necessary to strengthen the intervention of pain and psychological intervention of the children, strengthen the communication with the parents, find out the true cause and implement the intervention and implement the transitional care practice personally.

关键字 Limb fracture; Children; Parents; Psychological Experience;Transitional Care

分类：22. Psychology Mental Health 心理
1043

5-Aminolevulinic Acid Combined with Ferrous Iron Alleviates Chronic Stress-Induced Depression- and Anxiety-Like Behavior in Depressive Mice

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Background: Depression is a mental disease that significantly reduces the quality of patients' life. Around 322 million people of all ages carry the heavy burden of depression on a worldwide scale, with a life-time prevalence of 20% according to the WHO. The aim of the current study was to investigate the role of 5-Aminolevulinic acid (5-ALA) in treating depression. 5-ALA, an intermediate in heme synthesis, is fundamental for aerobic energy metabolism. Heme oxygenase (HO) -1 cleaves heme to form biliverdin, carbon monoxide (CO), and iron (Fe2+) , which is used with 5-ALA. Furthermore, previous studies demonstrated that 5-ALA exerts anti-oxidation and anti-inflammatory. However, the molecular mechanism of 5-ALA/SFC anti-depression effect is not clear.
Methods: A investigation to determine the effects of 5-ALA/SFC on improving depression- and anxiety-like behavior in a mouse model is performed, induced by 1 week chronic unpredictable mild stress (CUMS). 'Saline' (3ml), '5-ALA/SFC' (30mg/kg), '5-ALA/SFC' (100mg/kg) were administered to mice via the intraperitioneal route. We examined the anxiolytic effects of 5-ALA/SFC on mice behavior in the forced swimming test (FST) and open field test (OFT). The dopamine (DA), 5-hydroxytryptamine (5-HT), and norepinephrine (NE) in the hippocampus was measured with HPLC. The neuroinflammation and apoptosis was observed by the analysis of related cytokines.
Results: 5-ALA/SFC group showed greater benefits with respect to a reduction in the immobility time period and enhancement of 5-HT in the hippocampus, compared with SAL group which indicated that 5-ALA/SFC suppressed depression-like behavior. Moreover, 5-ALA/SFC group significantly upregulated the protein expression of brain-derived neurotrophic factor (BDNF), decreased cyclooxygenase-2 (COX-2), transient receptor potential vanilloid type 1 (TRPV1) and cannabinoid receptor subtype 1 (CB1) protein level in mice hippocampus. Further studies revealed that 5-ALA/SFC regulated immunity, monoamine systems by multi-target interactions, including inhibition of neuroinflammation and apoptosis.
Conclusion: Taken together, these findings suggested that 5-ALA/SFC has therapeutic effects in a mice depression model through increasing protein expression of BDNF, improving the anti-neuroinflammation and anti-apoptosis ability of the brain.

关键字 depression, anxiety, 5-aminolevulinic acid, mice

分类：22. Psychology Mental Health 心理
1044

Study on the Value of Children’s Depression Inventory for Early Detection of Depressive Symptoms in Children Hospitalized in Nephrology and Rheumatology Department

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Objective: To study the value of Children’s Depression Inventory (CDI) for early detection of depressive symptoms in hospitalized children with chronic kidney disease and rheumatoid arthritis .
Methods: One hundred and forty-four patients aged over 8 years who were hospitalized in the Department of Nephrology and Rheumatology were evaluated. These children were asked to fill out the CDI. The psychiatrist interviewed them and diagnosed according to DSM-5, and the parents were asked to fill out the Child Behavior Checklist (CBCL) and the questionnaire related to primary diseases (including diagnosis of primary disease, disease burden, situations of patients and their families). The correlations between the scales were analyzed. Results: The positive rate of depressive symptoms based on the CDI scale was 26.40%, and 29.2% of the children met the DSM-5 criteria for major depressive disorder. Positive DSM-5 was highly correlated with positive CDI （x2=98.981，p=0.000）. Medical examinations for primary diseases (OR=1.745, 95%CI=1.016-2.996, p=0.044) and disagreeable personality (or = 0.164,95% CI = 0.039-0.680, p = 0.013) were the risk factors for the diagnosis of depressive disorder.
Conclusion: Depressive symptoms are often found in hospitalized children with chronic kidney disease and rheumatoid arthritis, and medical examinations related to primary diseases and disagreeable personality are risk factors. More attention should be paid to these children. CDI can be used for early and rapid identification Depressive symptoms in children.

关键字 chronic kidney disease; rheumatism; children; emotion; depression

分类：22. Psychology Mental Health 心理
1097

Baduanjin as a Treatment for Hyperactive-Impulsive Symptoms of Attention Deficit Hyperactivity Disorder: study protocol for a randomized controlled trial.

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Background: Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders among school-aged children, characterized by age-inappropriate inattention and/or hyperactivity-impulsivity. Physical exercise is indicted as an alternative approach to the treatment of ADHD, used independently or complementary to medication or behavioral interventions that can yield both acute and lasting positive effects on executive function, which is known as the core neurobiological deficit in ADHD. Baduanjin exercise, a combination of physical exercise and Chinese qigong movement, is seen as a potential alternative treatment of ADHD in Traditional Chinese Medicine (TCM). This study aims to evaluate the effectiveness of Baduanjin exercise on reducing the hyperactive-impulsive symptoms of children with ADHD compared to routine excise as the control group. Investigators will also examine if the Baduanjin exercise will positively affect Traditional Chinese Medicine (TCM) symptoms compared to controls and if these impacts are related to the change of the executive function.
Method: The present study will be carried out using a parallel randomized study design. Participants will be 120 children and adolescents aged between 7years 0 months to 16 years 11months. Each participant will be randomly allocated either to the Baduanjin exercise intervention group or to the routine physical exercise control group in the ratio of 1:1. Both groups are asked to do the designated exercise for at least 30 minutes each day and at least 5 days each week for 3 months. The primary objective is to compare the Hyperactivity/Impulsivity score change in The Swanson, Nolan, and Pelham Questionnaire (SNAP-IV) Rating Scale at 3- and 6-months follow-up. The secondary objective of this study is to examine the change of Scoring evaluation of the TCM symptoms after 3 months of treatment and 6 months of follow-up. In addition, the mediating effect of executive function measured by both the Cambridge neuropsychological test automated battery(CANTAB) test and Behavior Rating Inventory of Executive Function, Second Edition(BRIEF-2) scale will be calculated. Furthermore, we will determine whether these effects extend to other ADHD-related problems, including the sensory integration score, Developmental Test of Visual Perception, and other behavioral problems. Follow-up measures will be collected 3 months and 6-months after the collection of baseline measures.
Results: This is an ongoing trial(NCT04282460). Therefore, the results of this trial have not been revealed.
Conclusions: This is the first rigorous evaluation of the Baduanjin exercise as an alternative treatment of ADHD and provides evidence as to whether it is more effective than routine exercise. The trial will provide important information on the effectiveness of this flexible and well-accepted home-based intervention for children and adolescents with ADHD. It will also examine potential mediating factors, especially the role of executive function.

关键字 Attention Deficit Hyperactivity Disorder, Chinese Traditional Medicine, Baduanjin Exercise, Executive Function

分类：22. Psychology Mental Health 心理
1104

The effects of maternal prenatal depression on child mental health: The moderating role of maternal childhood trauma

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2. 上海交通大学医学院附属精神卫生中心

Background: There is a large body of evidence suggesting that maternal prenatal depression significantly predicts mental health problems in children. However, evidence suggests that maternal prenatal depression is not the only factor influencing child development, with other prominent factors being identified, such as maternal childhood trauma. To date, little is known about the role of maternal childhood trauma within this effect. What's more, different types of childhood trauma may have diverse effects. Therefore, the current prospective study aimed to examine the effect of maternal prenatal depression on child mental health problems at 6 years of age, and the moderating effects of maternal childhood trauma. Considering that maternal prenatal depression and early trauma history may cumulate an increased risk of adverse child outcomes, we hypothesized that (1) maternal prenatal depression would have a negative impact on child mental health, and mothers' childhood trauma likely aggravate this adverse effect; (2) the cumulative effect probability varies depending on the different types of childhood trauma.

Method: The current study was part of the Shanghai Sleep Birth Cohort Study (SSBCS), a longitudinal and prospective mother-child cohort aiming to assess the long-term effects of maternal emotional state in the third trimester on child social and emotional development. A total of 431 pregnant women were recruited from May 2012 to July 2013. At 6-year postnatal (December 2018 to December 2019), 187 mother-child dyads were followed up (retention rate = 43.39%). The current study focused on the subsample of 187 mother-child dyads (maternal M_{age} = 29.44 ± 4.44; 51.3% boys, child Mage = 6.27 ± .14 years) with complete data.

Maternal prenatal depressive symptoms were evaluated during the third trimester (between gestational age ⩾28 weeks and delivery) with the total depressive symptom scores of the Chinese version of *Center for Epidemiological Survey-Depression Scale (CES-D)*. At the 6-year follow-up, mothers retrospectively reported on their adverse childhood experiences with the *Childhood Trauma Questionnaire (CTQ)* and child emotional and behavioral problems with the total difficulties scores of *Strengths and Difficulties Questionnaire (SDQ)*. The effects of maternal depression at late pregnancy on the child mental health at 6 years old were analyzed, with different types of maternal childhood trauma (emotional abuse, EA; physical abuse, PA; sexual abuse, SA; emotional neglect, EN; physical neglect, PN) being examined as moderators.

Results: The prospective study found intergenerational transmission of maternal prenatal depression in a general population after controlling for demographic variables (maternal age and education level, age and sex of children, family annual income) in all analytical models. There was a positive association between maternal prenatal depressive symptoms and mental health problems in children (β = .13, p < .05). More importantly, we extended existing research by discovering an interaction between maternal prenatal depression and childhood emotional abuse on child mental health (β = -.05, p < .05). Specifically, maternal prenatal depression significantly predicted child mental health problems only when the level of childhood emotional abuse was low (β = .19, p < .05); however, when the maternal childhood emotional abuse level was high, maternal prenatal depression did not have an impact on the child mental health (β = -.025, p = .751).

Conclusions: The findings provided new insights into the impact of maternal prenatal depression on child mental health, signifying that prevention and intervention efforts should prioritize mothers with prenatal depression and childhood trauma history.

关键字 maternal prenatal depression, childhood trauma, emotional abuse, child mental health

分类：22. Psychology Mental Health 心理
1284

Negative life events and adolescent non-suicidal self-injury: The mediating role of alexithymia and the moderating role of difficulties in emotion regulation

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Objective: To investigate (a) the mediating role of alexithymia in the association between negative life events and adolescent NSSI, and (b) the moderating role of difficulties in emotion regulation in the indirect relationship between alexithymia and adolescent NSSI. Methods: A total of 183 (mean age = 13.14 years, SD = 1.55) adolescents from Beijing and Shandong were assessed with the Ottawa self-injury inventory (OSI), Adolescent self-rating life events checklist (ASLEC), Toronto Alexithymia Scale (TAS-20) and Difficulties in Emotional regulation scale (DERS). Results: The correlation analyses indicated that negative life events, alexithymia, difficulties in emotion regulation and adolescent NSSI were significantly positively correlated with each other. The effect of negative life events on adolescent NSSI was found to be partially mediated by alexithysia, and the indirect effect of the mediation model was moderated by difficulties in emotional regulation, the mediated path was stronger for adolescents with more difficulties in emotion regulation. Conclusion: Alexithymia has a partial mediating effect on the relationship between negative life events and adolescent NSSI, and the effect was significantly moderated by difficulties in emotion regulation.

关键字 NSSI, Negative life events, Alexithymia, Emotion regulation

分类：22. Psychology Mental Health 心理
1293

Mental health problems in young children aged 3 and 4 years in China from 2016 to 2020: Trends and decomposition analysis of social determinants

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Background

Mental health is an indispensable component of the UN Sustainable Development Goals and the Healthy China 2030 agenda. When devising policy to promote mental health and early childhood development, it is key to know specific contribution from various social determinants. Yet little is known about how these factors alone or in combination are responsible for young children's mental health trend. The current study examined whether young children's mental health problems have changed from 2016 to 2020 and investigated the social determinants and their relative contribution to these changes.

Method

The current study utilized data from the Shanghai Children's Health, Education and Lifestyle Evaluation, Preschool (SCHEDULE-P) study. Five waves of data on newly enrolled kindergarteners from 2016 to 2020 were collected. The final sample included children aged 3 and 4 years recruited in 2016 (n=20 271), 2017 (n=21 820), 2018 (n=23 662), 2019 (n=25 301), and 2020 (n=26 610).

Child mental health problems were assessed by the Strengths and Difficulties Questionnaire. The following social determinants were collected: The 2016-2020 per capital GDP for each district in Shanghai was retrieved from the Shanghai Statistics Bureau to represent population-level socioeconomic status (SES). Mothers' and fathers' education level and household income were self-reported as individual-level SES. Parents reported on child age and gender, single child status, the primary caregiver, and child screen use in the past month. Child's sleep was assessed by Children's Sleep Habits Questionnaire. Parent-child interaction was assessed using the Chinese Parent-Child Interaction Scale. Harsh parenting was assessed by the frequency of physical abuse in the past week.

Descriptive statistics were obtained for each wave to describe child mental health trend. Overall differences of mental health across five waves were run with ANOVA, with Bonferroni corrections applied for post-hoc pair-wise comparison. A series of Blinder–Oaxaca decomposition models was applied, with one SDQ scale entered as the dependent variable, with the following variables being entered as factors: mother's education level, father's education level, annual household income, per capital GDP, parental vs. non-parental care, status of single child, child media use, child sleep duration, child sleep disturbance, parent-child interaction, and harsh parenting.

Results

There were secular improvements in overall mental health problems, as well as in emotional symptoms, conduct problems, peer problems, hyperactivity problems, and prosocial behaviors in Chinese preschoolers aged 3 and 4 years from 2016 to 2020. Decomposition models suggested that proposed social determinants explained 66.68%, 58.49%, and 74.27% of the changes in overall mental health, internalizing symptoms,

and externalizing symptoms between 2016 and 2020, respectively. For overall mental health change between 2016 and 2020, parent-child interaction, single child status, and family income were identified as the top contributing factors. For internalizing symptoms, parent-child interaction, family income, and mothers' education level were the top contributing factors. For externalizing symptoms, parent-child interaction, single child status, and sleep problems were the top contributing factors.

Conclusions

The current study revealed overall improvements of child mental health from 2016 to 2020. Changes in parent-child interaction was identified as the most important predictors of mental health changes. Family income and mothers' education level matter more in predicting internalizing symptom changes, and single child status and sleep problems contribute more to externalizing symptom changes. The findings offer valuable information in understanding the up-to-date secular trend in mental health problems and associated factors, and thus inform policy efforts for prevention and intervention to promote early childhood development.

关键字 Mental health, preschooler, secular trend, social determinant

分类：22. Psychology Mental Health 心理

1370

Relationship between Impulsivity and Alexithymia in Adolescent with Nonsuicidal Self-injury

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Objective: To explore the relationship between impulsivity and alexithymia in adolescents with NSSI.

Methods: A total of 67 (mean age = 12.30 years, SD = 1.93) adolescents from Beijing Anding Hospital were assessed with the Ottawa Self Injury Scale (OSI), Barratt Impulsivity Inventory (BIS-11) and Toronto Alexithymia Scale (TAS-20).

Results: (a) The scores of BIS-11 and TAS-20 and the scores on most of factor (except for the attention impulse and the the extraverted thinking) were significantly higher in NSSI frequent group than the occasional group.

(b) The total score of BIS-11 was significantly positively correlated with the total score of TAS-20 ($r=0.474$, $P<0.01$), the emotion recognition factor ($r=0.42$, $P<0.01$) and the extroverted thinking factor ($r=0.47$, $P<0.01$). Regression analysis indicated that the total score of TAS-20 and score of the emotion description failure factor predicted total score of BIS positively, in contrast, extroverted thinking factor predicted total BIS score negatively. These could explain 34% of the variation of the total BIS score.

Conclusion: Alexithymia in adolescents with NSSI could significantly predict the impulsivity, and high levels of alexithymia and impulsivity may lead to more frequent NSSI behaviors.

关键字 Adolescent;Impulsivity;Alexithymia

Category: 22. Psychology Mental Health 心理

1451

What is the Role of Resilience from Adversities Experienced Among Rural Youth Attempting to Academically Thrive in China?

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Abstract Content Although resilience can play an important role in enabling students who face adverse social circumstances to succeed academically (Martin & Marsh, 2006), few studies have explored resilience and its association with academic performance among disadvantaged rural students in developing countries (Mwangi et al., 2018). In the current study, we measure the association between student resilience and academic performance as well as the psychosocial correlates of these two outcomes in a poor area of rural China.

Methods Our sample included 1,609 students in 30 primary and lower secondary schools in a rural region of Gansu province, which is a low-income area located in northwest China. To measure the resilience levels of children and their caregivers, we used the internationally validated 25-item Connor-Davidson Resilience Scale (CD-RISC), and to measure academic performance we used a 30-minute standardized math test. To carry out the analysis, we conducted t-tests to identify which factors were associated with higher levels of resilience and academic performance, and we used an ordinary least square (OLS) linear regression model to conduct the multivariate analysis.

Results We found that the mean resilience score of the sample students was 59.87 (mean CD-RISC score = 59.87, standard deviation = 14.22), which is lower than the mean scores reported in almost all other identified studies of similarly aged students both inside and outside of China. Protective factors of student resilience included caregiver resilience (mean CD-RISC score = 55.36, standard deviation = 18.91), mother’s education level, reading time, and active participation in group-based activities at school, while risk factors included low perceived social support, female gender, being bullied monthly or more, and screen time exceeding one hour. Additionally, a one-point increase in the CD-RISC was associated with a 0.02 SD increase in math score ($p<0.001$), and the math scores of students whose CD-RISC were in the bottom quartile were 0.45 SD lower than those of their peers ($p<0.001$). The strong and positive association between student resilience level and academic performance persisted even when controlling for other factors.

Conclusion Our study highlights the strong link between the resilience and academic performance in disadvantaged contexts, and it sheds light on the assets and resources that may lead to higher levels of student resilience in at-risk communities. Potential implications for policy involve the need to identify interventions that take context-specific, multisystemic approaches to improving the access of at-risk students to protective resources such as social support and pro-social activities, with the ultimate aim of increasing student resilience and ultimately their chances at success in school and in life.

Key words resilience, adversity, academic performance, school-age students, rural China

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Category: 22. Psychology Mental Health 心理
1452

Planting seeds for resilience: A pilot mindfulness and mentorship program in migrant Chinese children

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2. Fudan University

Abstract Content Mental health problems affect 1 in 5 young people and is the leading cause of disability worldwide. Evidence is lacking in low-and-middle-income countries where 90% of the affected youth lives. Statistically, every 1 in 8 young people lives in China. Chinese rural-to-urban migrant children are at high risk for mental health issues due to socio-educational disruptions, poor resource access and stigma. Mindfulness-based interventions in children have shown promise in developed countries to decrease depression and anxiety symptoms but trials are lacking in low-resource settings.

Methods Using a randomized controlled design, we piloted a volunteer-lead, 8 weekly-sessions-based Mindfulness program (N=285, 44%) vs. waitlist control (N=368, 56%) in 9-14 years-old migrant Chinese children, delivered by trained community volunteers in 2020. We examined the groups in their socio-economic factors, mindfulness (MAAS), resilience (SDQ and CD-RISC), depression (CES-D) and anxiety (MASC) scores at baseline and post intervention. Multivariable regression analyses and student t-tests were used to compare between group differences and assess associations at each time point.

Results At baseline, there was no significant differences between the control group and the intervention arms. After 8 weeks of intervention, no significant differences were found between the intervention vs. control arms in Mindfulness scores (63.6±1.15 vs. 63.7±0.83, $p>0.05$), resilience scores (12.4±0.57 vs. 11.5±0.33, $p>0.05$), anxiety scores (41.5±1.99 vs. 40.8±1.23, $p>0.05$) or depression scores (11.1±1.20 vs. 10.6±0.74, $p>0.05$). Being female and not having a personal cell phone were associated with higher anxiety scores. Three-month follow up data and qualitative data are being finalized for understanding these preliminary post-intervention results.

Conclusion A community volunteer-led, 8-week Mindfulness prevention program adapted from existing literature did not significantly impact migrant Chinese student Mindfulness, resilience, anxiety, or depression levels. More research is needed for developing effective mental health preventive programs specific to resource-limited settings.

Key words China, Migrant Children, Resilience, Mental Health, Mindfulness
Reference N/A

分类：22. Psychology Mental Health 心理
1466

Identify abnormal white matter across neurodevelopmental disorders: a meta-analysis of diffusion tensor imaging studies

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Background: Neurodevelopmental disorders (NDDs) include attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), motor disorder, communication disorder, intellectual disability and specific learning disorder, are known to be both clinically and pathophysiologically overlapped. NDDs are not distinct entities, rather, NDDs often present overlapped clinical symptoms, share genetic and neuroimaging changes. Diffusion tensor imaging (DTI) is a novel neuroimaging technique that can detect white matter microstructure in vivo. According to previous DTI studies, white matter disfunction are suggested to be responsible for NDDs. Studies focus on common and distinct white matter patterns in NDDs will provide further insight to both etiology and nosology.
Objective: To identify consistent white matter microstructural abnormalities in each NDD, and further investigate common and distinct abnormal patterns across NDDs.
Methos: A comprehensive literature search was conducted up to 11th March 2020 to identify studies that compared fractional anisotropy (FA) or mean diffusivity (MD) between individuals with NDDs and neurotypical subjectes. Peak coordinates were generated and meta-analyzed via two coordinate based meta-analysis methods, Anisotropic effect size-signed differential mapping (AES-SDM) as well as activation likelihood estimation (ALE). Publication bias was evaluated by funnel plot and Egger's test.
Results: 66 studies were identified and further analyzed. FA reductions were found in the splenium of CC in both ASD and ADHD. A wider pattern was found in ASD compared with ADHD, with FA reductions in the genu of CC and MD increases in the right posterior thalamic radiation, retroleticular part of internal capsule and corona radiata were identified. No significant FA nor MD changes were detected in other NDDs. In the examination of pooled NDDs, FA reductions were found in the body, genu and splenium of CC.
Conclusions: The current study unveils disease-specific neural substrates among NDDs, provides insights into overlapped and unique pathophysiology underlying these conditions and encourages further investigations.

关键字 white matter, ASD, ADHD, neurodevelopmental disorders, DTI

Category: 22. Psychology Mental Health 心理
1482

Depression, anxiety, and caregiver burden among adult caregivers of pediatric patients with neurodevelopmental disorders: A descriptive cross-sectional study

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Abstract Content Background: The increasing prevalence of neurodevelopmental disorders in children generates a major impact on the lives of their families. In particular, the caregivers of these children have demanding experiences which may lead to the development of depression and anxiety. However, the presence and severity of these psychological disorders may be affected by factors such as spirituality, caregiver burden, and the specific neurodevelopmental disorder of the child. This study seeks to determine the prevalence of depression and anxiety among caregivers of pediatric patients with neurodevelopmental disorders seen at the UERMMMCI Pediatrics Outpatient Department. It likewise seeks to examine factors associated with depression and anxiety among the caregivers. These factors include the demographic profile of the caregivers (age, marital status, gender, religion, educational attainment, and employment status), diagnosis of the patient, level of caregiver burden, parenting practices, and spirituality scores.

Methods Methods: This is a cross-sectional study conducted at the University of the East Ramon Magsaysay Memorial Medical Center Inc. (UERMMMCI) Pediatrics Outpatient Department from October 2017-March 2018. Data gathered was summarized using descriptive statistics and measures of central tendency. Associations between variables were determined using chi-square analysis, subgroup analysis, and independent T-tests. SPSS v 23.0 was used for all statistical analysis of data.

Results Results: Findings of the study showed significant correlations between caregiver anxiety scores and the specific diagnosis of the child they care for. Depression scores ($p<0.001$) were likewise correlated with the diagnosis of the child ($p=0.006$). On the other hand, caregiver burden ($p<0.001$) was found to be correlated to caregiver education ($p=0.008$) and the duration of the child's illness ($p=0.004$). A striking finding is a positive correlation between anxiety levels, depression scores, and caregiver burden. This coincides with many studies which show the interplay between the 3 factors. No correlation was found between these 3 factors and spirituality.

Conclusion Conclusion: Results of the study have implications in terms of addressing caregiver burden, as decreasing anxiety and/or depression levels through various forms of therapy may ease the stress of these caregivers. This may also serve as a springboard in future research in terms of the effect that the caregiver's mental state may have on the child they care for.

Key words depression, anxiety, caregiver burden, pediatric patients, neurodevelopmental disorders, adult caregivers

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eNOS regulates retinopathy and vascular permeability in the animal model of retinopathy of prematurity

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Abstract Content Objective: The incidence of vision-threatening retinopathy of prematurity (ROP) in children is increasing due to well-managed neonatal care. Edema due to leaky blood vessels in the affected retina contributes to tissue deterioration and vision loss. Therapeutics targeting vascular endothelial growth factor (VEGFA) suppress leakiness and edema but do not resolve the underlying hypoxia and may cause disease progression. Therefore, there is a clinical need to develop more refined therapeutics. The objective of this study was to determine to what extent and how VEGFA ‘s effect on leakiness is dependent on nitric oxide (NO), in order to understand the molecular mechanisms underlying pathological edema in ROP.
Methods Methods: Here, we have examined the role of endothelial NO synthase (eNOS) activity in pathological neovascularization and vessel permeability during oxygen-induced retinopathy in mice, which is known as an animal model of ROP. NO formation was suppressed chemically by L-NMMA,or genetically, in the catalytically inactive mouse strain (Nos3S1176A/S1176A).
Results Results: In both cases resulting in reduced formation of pathological neovascularization. Mechanistically, the consequence of NO suppression was manifested at endothelial junctions by 1) reduced levels of eNOS and active c-Src at junctions, 2) reduced levels of phosphorylation of Y685 in vascular endothelial (VE)-cadherin, associated with VEGFA-induced permeability, and 3) reduced vascular leakage.
Conclusion Conclusions: eNOS activity in endothelial cells leads to destabilization of adherens junctions and increased vascular permeability by converging with the c-Src-VE cadherin pathway known to operate in VEGFA-regulated permeability. Thus, eNOS is an important target for the development of therapeutic agents to treat ROP.

Key words Retinopathy of Prematurity, VEGF, eNOS, VE cadherin
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Effect of Neonatal neuronal intensive care unit on neonatal encephalopathy

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Abstract Content Prophylaxis of brain injury in newborns has been a main concern since the first neonatal neuronal intensive care unit (NNICU) in 2008. The aim of this study was to outline the unit’s development and analyze the demographics of the patients, the services delivered, the short-term outcomes before and after the establishment of NNICU.

Methods The medical records of neonates who were suspected neonatal encephalopathy or had primary medical diagnosis known to be associated with neurologic compromise during the study periods were collected. The study period from 2011.03.01 to 2012.09.30 was the 18-months pre-NNICU and the period from 2018.03.01 to 2019.09.30 was the 18-months post-NNICU.

Results During the two investigation periods, 384 newborns were diagnosed or suspected as “neonatal encephalopathy”, of which 185 patients admitted before the establishment if NNICU, another 199 neonates enrolled in post-NNICU group. Patients in the post-NNICU group were more likely to have seizures (P=0.001), incomplete or absent primitive reflexes (P=0.002), therapeutic hypothermia (P<0.001) and liquid control (P<0.001) in acute phase. Meanwhile, amplitude-integrated electro encephalogram (aEEG) monitoring (P<0.001) and cranial ultrasound (P<0.001) were more often used in NNICU. Both of the follow-up rate in brain MRI and the assessment of neurodevelopment at 3 months were higher in the post-NNICU group (P<0.001).

Conclusion The establishment of NNICU focused on the neonatal neurocritical care for the babies susceptible to NE, with the guidance of evidence-based medicine, the NNICU of CHCMU is gradually improving and standardizing the neuroprotective therapy and clinical follow-up to improve neurodevelopmental prognosis of the NE patients.

Key words neonatal encephalopathy, neonatal, neonatal neuronal intensive care unit, neuroprotective strategies.

Reference

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Human oligodendrocyte progenitor cells transplantation reduce white matter injury in preterm goat fetus

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Purpose: White matter injury (WMI) is the main form of brain injury in preterm infants. Oligodendrocyte progenitors (OPCs) are predominantly damaged when suffering from WMI. In this study, human OPCs were transplanted in the fetal goat model of preterm WMI. The differentiation capacity of transplanted OPCs and their ability to alleviate fetal WMI were examined.
Methods: Pregnant ewes underwent surgery at 0.7 gestation. A catheter was implanted into the nasal cavity of the fetus and an inflatable balloon occluder was placed around the umbilical cord. Umbilical cord occlusion (UCO) was administered three days after the surgery to cause hypoxia ischemia. Twenty million human OPCs labeled with fluorescent dye CM-DiI, or saline, was intranasally administered 12 h after acute hypoxia-ischemia insult. Brains were collected 14 days or 21 days later for histological assessment. Pathological changes were detected by Hematoxylin and Eosin (H&E) staining. NG2, MBP, and MAG were double-labeled with CM-Dil to assess the differentiation of transplanted OPCs. Western blot and immunofluorescence staining of MBP and MAG were used to detect mature oligodendrocytes. The ultrastructure of myelin sheath was examined by transmission electron microscope. The proliferation ability of transplanted OPCs were assessed through Ki-67 staining.
Results: UCO induced white matter injury in preterm goat fetus. H&E staining indicated glial scars and loosened fibers in brain white matter. Immunofluorescence staining showed a reduction in MBP+ and MAG+ myelin fiber density compared to control fetuses. Western blot also revealed decreased MBP and MAG level in the UCO group. The transplanted OPCs still survived 14 and 21 days after transplantation. Immunofluorescent staining showed that they expressed MBP and MAG, but barely expressed NG2, proving their ability of differentiation. The myelin density (MBP+ or MAG+) was increased in OPCs treatment group compared with saline group. The transmission electron microscope revealed that the number of myelinated nerve fibers were increased in OPC treatment group. Moreover, immunofluorescent staining showed that transplanted OPCs barely express Ki67, suggesting a low risk of tumorigenicity.
Conclusion: Exogenous OPCs survived after transplantation and differentiated into mature oligodendrocytes. OPCs transplantation alleviated WMI induced by hypoxia ischemia.

关键字 White matter injury; Oligodendrocyte progenitor cells; Transplantation

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Regulation of TLR9 on pyroptosis, apoptosis, and necroptosis through p38 MAPK signaling pathway in a neonatal rat model with sepsis associated encephalopathy

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Aims: Sepsis, a serious disease with a high mortality, usually causes sepsis associated encephalopathy (SAE). The underlying pathology of SAE is complex and involves different types of cell death. As an inflammation-related protein, Toll-like receptor 9 (TLR9) often causes cell death and organ damage, but it has rarely been studied in SAE.
Methods: A rat model of SAE was established by cecal ligation and perforation (CLP). Rats were randomly divided into different groups and given TLR9 inhibitor ODN2088, p38 mitogen-activated protein kinase (MAPK) kinase inhibitor SB203580, extracellular signal-regulated kinase (ERK) kinase inhibitor PD98059, Jun N-terminal Kinase (JNK) kinase inhibitor SP600125, and necroptosis inhibitor NEC-1s immediately after CLP. Survival and vital signs were monitored and neurobehavioral scores were assessed. Pathological changes of cortex were observed by HE staining. Apoptosis, pyroptosis, and necroptosis-related proteins were detected by western blotting. The expression of TLR9 was determined by western blotting and immunofluorescence staining. The ultrastructure of neurons was observed under transmission electron microscope.
Results: After CLP, survival rate of rats decreased, vital signs deteriorated, neural reflex was retarded, and cortical pathological changes were serious, indicating that CLP successfully induced SAE. Nerve cells in the cortex of CLP showed apoptosis, pyroptosis, and necroptosis, and p38 MAPK, ERK and JNK signaling pathways were all activated. MAPKs inhibitors were administrated, only p38 MAPK inhibitor simultaneously regulated apoptosis, pyroptosis, and necroptosis, that is, they inhibited apoptosis and pyroptosis, but activated necroptosis. TLR9 was also activated in the CLP-induced cortex of rats. Inhibition of TLR9 inhibited p38 MAPK and ERK signaling pathways, as well as apoptosis, pyroptosis, and necroptosis. In addition, inhibition of TLR9 also improved the survival rate of CLP-induced SAE rats and reduced the cortical pathological changes.
Conclusions: Our findings suggested that TLR9 regulates apoptosis, pyroptosis, and necroptosis through the p38 MAPK signaling pathway in SAE, and necroptosis has a regulatory effect on apoptosis and pyroptosis. TLR9 is one of the causes of SAE, and effective inhibition of TLR9 can play a neuroprotective role.

关键字 sepsis associated encephalopathy, TLR9, apoptosis, pyroptosis, necroptosis, p38 mitogen‐activated protein kinase

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Extreme ambient temperature exposure during pregnancy —outcome and mechanism

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Background: When global warming continues, increased countries will suffer from extreme ambient temperature in the future. Literatures have suggested that extreme ambient temperature may associated with adverse pregnancy outcomes such as low birth weight, premature birth and stillbirth.
Objective: A review was conducted to better understanding the influence and mechanism of extreme ambient temperature on pregnant women and their offspring.
Result: Extreme ambient temperature might act as a stressor which can change hormone levels and blood flow distribution in pregnant women. Moreover, extreme ambient temperature changes alter the methylation level of the related genes, increasing the incidence of chronic diseases in offspring, such as hypertension. These changes lead to the decline of placental function and lead to the occurrence of adverse maternal and neonatal outcomes. Extreme ambient temperature exposure in susceptible period could cause low birth weight, preterm, stillbirth and even hypertensive disorder complicating pregnancy. Besides, fetus suffered extreme ambient temperature exposure in critical period of development might influence their health in adulthood.
Conclusion: Pregnant women and the offspring are susceptible to heat and cold exposures. Pregnant women who suffer from these exposures are at a higher risk of developing gestational diseases, such as preterm birth, stillbirth, and eclampsia. Furthermore, the offspring are at higher risk for LBW and birth defects. Pregnant women should avoid exposure to extreme ambient temperature to ensure the health of their mothers and children.

关键字 Key words: ambient temperature; pregnancy; offspring; birth weight; gestational disorders

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The vertical transmission of virus infection through breast milk

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Objective: To summarize the research advances in the vertical transmission of 7 common viruses through human breast milk.
Methods: Breast milk is conducive to the growth and development of infants, but it may also carry viruses and harm infants by breastfeeding. At present, the vertical transmission of most virus infections through breast milk has not been determined. PubMed, Embase, CNKI, Weipu Database, and Wanfang Database were searched for related studies published from January 1, 2015 to November 1, 2020.
Results: This study summarized the research progress in the vertical transmission of 7 common viruses through breast milk and provide a reference for clinicians and mothers who make feeding decisions. However, some references are derived from abroad and may not applicable to Chinese mothers and infants. The research of COVID-19 are mostly derived from the reports of pregnant women in the middle and late pregnancy, and the research are case series and case report, the level of which is low.
Conclusion: It is suggested that clinicians should combine professional knowledge and needs of patient to evaluate benefits of breastfeeding and apply them to the clinical practice prudently.

关键字 virus; breastfeeding; vertical transmission

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The Validity and Safety Assessment for Melatonin Use in Neonatal Hypoxic Ischemic Encephalopathy (HIE)

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Aim: Hypoxic ischemic encephalopathy (HIE) is one major cause of neonatal acute death and chronic neurological damage, the treatment of which still the most concerned. After Therapeutic Hypothermia, the most common treatment for HIE, there still remained many adverse outcomes. Melatonin is a natural hormone and can act as a powerful antioxidant and anti-apoptotic agent, already demonstrated to be a protector in such neural injury. But its validity and the safety still need more evidences to approve.
Method: A literature search was completed from Medline, Ovid, Embase, Google Scholar, PubMed, Cochrane central databases of Systematic Review, published journals, conference proceedings, and other database. The included articles were published within the past 10 years, 2011-2021.
Result: Melatonin use can help improve the outcome of HIE neonates.
Conclusions: Melatonin can be effective in HIE treatment. But it still needs to be validated in larger randomized controlled trials.

关键字 Hypoxic ischemic encephalopathy (HIE); Melatonin; Neonatal;
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Mild Hypothermia Combined With RhFGF21 Play A Neuroprotective Effect After Hypoxia-Ischemia Brain Injury in Neonatal Rats By Regulating AMPK-Sirt1-mTor Signaling Pathway

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Neonatal hypoxic-ischemia (HI) is a serious and difficult problem that urgently needs prevention and treatment during the perinatal period. At present, there is no specific medicine to alleviate the dysfunction after HI. The only clinical treatment method is mild hypothermia treatment. The previous research of our research group found that human-derived recombinant fibroblast growth factor 21 (rhFGF21) exerts an effective neuroprotective effect on hypoxic-ischemic brain damage. However, whether the combination of mild hypothermia (33℃~35℃) and rhFGF21 has a synergistic neuroprotective effect on neonatal hypoxic ischemic encephalopathy and its mechanism is still unclear. The experimental aim is to explore whether the combination of mild hypothermia (33℃~35℃) and rhFGF21 has a synergistic neuroprotective effect on neonatal hypoxic ischemic encephalopathy. We use Laser Speckle Contrast Imaging to observe changes in cerebral blood flow after HI. The cerebral infarct volume of rats in each group was measured and compared by the 2,3,5-Triphenyltetrazolium chloride staining (TTC) staining. Seven days after HI injury, the brain tissue structure, changes in cell arrangement, and changes in the number of Nissl bodies of the sham group, the HI group, the single rhFGF21 treatment, the single hypothermia treatment, the combination treatment were observed by HE staining and Nissl staining. Observe the expression of MAP2 by immunohistochemical staining. The expression of autophagy-related proteins was detected by Western blot analysis. Morris water maze test was used to detect the long-term learning and cognitive function of rats. The apoptosis of each group was observed by TUNEL staining. After transfection of mRFP-GFP-LC3 virus to primary neurons, the changes of autophagic flux in each group were observed and evaluated. Observe the expression of MAP2 and Sirt1 of each group of primary neurons by immunofluorescence analysis. In this study, both *in vivo* and *in vitro* models were used to evaluate whether mild hypothermia (33℃~35℃) combined with rhFGF21can play a synergistic neuroprotective effect after HI, and to explore related mechanisms. The results of the study demonstrated that mild hypothermia (33℃~35℃) combined with rhFGF21 treatment significantly reduced the level of cerebral edema (brain atrophy), reduced the area of cerebral infarction, improved the weight loss of neonatal rats after HI, and improved the structure of brain tissue. At the molecular level, the single rhFGF21treatment, the single mild hypothermia treatment and the combination therapy can reduce excessive autophagy and autophagy flux after HI. In terms of long-term efficacy, the treatment of mild hypothermia (33℃~35℃) combined with rhFGF21 21 days after HI accelerated the speed of finding the platform in the Morris water maze test and raised the number of platform crossings in the Morris water maze withdrawal test which were all better than the two single treatments. The Sirt1 inhibitor EX-527 can partially reverse these therapeutic effects mentioned above. In *in vitro* experiments, mild hypothermia (33℃~35℃) combined with rhFGF21 treatment can protect primary cortical neurons from oxygen-glucose deprivation (OGD) by inhibiting excessive neuronal autophagy, blocking autophagic flow, and then reducing apoptosis. Our animal and cell results revealed that mild hypothermia (33℃~35℃) combined with rhFGF21 can activate Sirt1 and inhibit neuronal autophagy by regulating the AMPK-mTor signaling pathway. Therefore, mild hypothermia (33℃~35℃)

combined with rhFGF21 may be a therapeutic method to promote the functional recovery of neonatal brain injury caused by HI.

关键字 rhFGF21; HIE; AMPK; Sirt1; autophagy

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TERT promotes neurogenesis and neural repair after hypoxic ischemic brain damage in neonatal rats

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Aim: To investigate the role of TERT in the regulation of neurogenesis after hypoxic-ischemic brain damage (HIBD) in developmental stage.
Method: We established a model of HIBD in neonatal rats both in vivo and in vitro, and used lentivirus and adenovirus transfection to increase the expression of TERT. We use TUNEL, CCK8 assay, immunofluorescence staining, and western blotting to detect the apoptosis, proliferation, migration, and differentiation of neural stem cells (NSCs). Neurobehavioral tests including Morris water maze test and the modified neurological severity score (mNSS) were conducted to evaluate the neurological function of neonatal rats after HIBD.
Results: We found that TERT attenuated apoptosis and promoted proliferation, migration, and differentiation in neural stem cells (NSCs). Furthermore, TERT induced myelination in the brain of neonatal rats after HIBD. Neurobehavioral tests revealed that TERT can improve learning, memory, and neurological function after HIBD in neonatal rats. In addition, we found that TERT may regulate neurogenesis after HIBD through the Sonic Hedgehog/Gli1 signaling pathway.
Conclusion: Our study demonstrated that TERT could promote neural repair and neurological function after hypoxic ischemic brain damage in neonatal rats. The new neuroprotective pathway regulated by TERT during HIBD described here could provide a basis for developing therapeutic strategy for neonatal HIE. Furthermore, TERT may be a potential target during neural repair and reconstruction in various diseases affecting nervous system.

关键字 telomerase reverse transcriptase, neurogenesis, neural repair, hypoxic ischemic brain damage, neonate

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Congenital toxoplasmosis with severe jaundice, splenomegaly, and pancytopenia: a case report and literature review

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Background:
Most infants infected with Toxoplasma gondii are completely asymptomatic at birth, yet they may develop ocular and neurological sequelae in the first few months of life. Cases of congenital toxoplasmosis with severe jaundice early after birth combined with pancytopenia and splenomegaly are extremely rare. Here, we report a rare case of congenital toxoplasmosis presenting with severe jaundice and hemolysis early after birth combined with pancytopenia and splenomegaly.
Case presentation: A male preterm infant with severe jaundice and splenomegaly was admitted to our department. Laboratory examinations revealed severe hyperbilirubinemia, increased reticulocytes, and pancytopenia. After comprehensive analysis and examination, the final diagnosis was congenital toxoplasmosis, and the infant was treated with azithromycin and subsequently trimethoprim-sulfamethoxazole. Regular follow-up revealed congenital toxoplasmosis in both eyes, which was surgically treated, while neurofunctional assessment results were unremarkable. In this case of congenital toxoplasmosis combined with severe jaundice, we treated the infant with two courses of azithromycin, followed by trimethoprim-sulfamethoxazole after the jaundice resolved. Clinical follow-up indicated that this treatment was effective with few side effects; thus, this report may serve as a valuable clinical reference.
Conclusions: Timely diagnosis and adequate treatment are closely associated with congenital toxoplasmosis-related prognosis. Infants with congenital toxoplasmosis require long-term follow-up, focusing on nervous system development and ophthalmology.

关键字 Congenital toxoplasmosis; jaundice; pancytopenia; splenomegaly; case report

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Research progress of hyperoxia -induced injury of pulmonary vascular endothelial cells in bronchopulmonary dysplasia

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Bronchopulmonary dysplasia (BPD) is common in premature infants who need oxygen therapy, and the main target cells of hyperoxia stress response are pulmonary vascular endothelial cells. This paper briefly reviews the change of the physiological function, metabolic process and messenger molecule of pulmonary vascular endothelial cells induced by hyperoxia in the development of BPD.

关键字 Bronchopulmonary dysplasia; Lung; Endothelial cells; Vascular remodeling; Hyperoxia; Etiology; Infant, premature
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Cases report of two infants of intestinal failure-associated liver disease treated with parenteral fish oil and literature analysis

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Object: To explore the prospect of fish oil intralipid in the treatment of intestinal failure-associated liver disease (IFALD). Method: We report two infants with IFALD who were treated with pure fish oil intralipid, and then the damage of liver function reversed. One infant needed long-term parenteral support due to small for gestational age, heart failure caused by symptomatic patent ductus arteriosus, and poor feeding tolerance. The other infant was complicated with severe neonatal necrotizing enterocolitis. Fish oil intralipid containing omega-3 was used to replace soybean oil intralipid after IFALD occured. Result: The liver function indexes of the two cases were significantly improved. Parenteral nutrition was stopped when they were discharged. Regular follow-up showed that the growth and development indexes were good. Conclusion: Combined with the analysis of relevant literature, the use of fish oil intralipid may be an effective method to prevent liver function damage caused by intestinal failure.

关键字 intestinal failure-associated liver disease; fish oil; direct bilirubin; intralipid

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Hyperlactemia caused by congenital hypothyroidism: a case report and literature analysis

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Object: To explore the etiological relationship between congenital hypothyroidism and hyperlactemia. Hyperlactemia can be caused by tissue hypoxia and other causes. If it is not treated in time, it is often life-threatening. When cardiac insufficiency or even heart failure occurs, it often leads to tissue hypoperfusion and hyperlactemia. Heart failure caused by congenital hypothyroidism is rare, and it is not often considered as the etiological differential diagnosis of hyperlactemia caused by heart failure, but if it is not removed in time, it will lead to serious consequences. Method: We report a case of congenital hypothyroidism in a child with heart failure and hyperlactemia. The child had abdominal distension, tongue vomiting, TSH exceeding the upper limit of detection, lactic acid up to 27 mmol/L, laboratory results also showed abnormal thyroid antibody. We use exogenous thyroxine supplement therapy and other adjuvant treatment measures. Result: After thyroxine treatment, lactic acid was quickly corrected, thyroid function and systemic symptoms were gradually improved, and the patient was cured and discharged. Conclusion: Pediatricians should be vigilant when facing neonates, especially premature infants, with corresponding symptoms of hypothyroidism, heart failure and hyperlactemia, actively look for the causes of thyroid function, and timely intervene to improve the prognosis of children.

关键字 Hyperlactemia; congenital hypothyroidism; heart failure
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Predictive value of early amplitude integrated electroencephalogram (aEEG) in sleep related problems in children with perinatal hypoxic-ischemia (HIE)

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Abstract
Background: While great attention has been paid to motor and cognitive impairments in children with neonatal Hypoxic-Ischemic Encephalopathy (HIE), sleep related circadian rhythm problems, although commonly present, are often neglected. Subsequently, no early clinical indicators have been reported to correlate with sleep-related circadian dysfunction during development.
Methods: In this study, we first analyzed patterns of the amplitude integrated electroencephalogram (aEEG) in a cohort of newborns with various degrees of HIE. Next, during follow-ups, we collected information of sleep and circadian related problems in these patients and performed correlation analysis between aEEG parameters and different sleep/circadian disorders.
Results: A total of 101 neonates were included. Our results demonstrated that abnormal aEEG background pattern is significantly correlated with circadian rhythmic (r=0.289, P=0.01) and breathing issues during sleep (r=0.237, P=0.037). In contrast, the establishment of sleep-wake cycle (SWC) showed no correlation with sleep/circadian problems. Detailed analysis showed that summation of aEEG score, along with low base voltage (r=0.272, P=0.017 and r=-0.228, P=0.048, respectively), correlates with sleep circadian problems. In contrast, background pattern (BP) score highly corelates with sleep breathing problem (r=0.319, P=0.004).
Conclusion: Abnormal neonatal aEEG pattern is correlated with circadian related sleep problems. Our study thus provides novel insights into predictive values of aEEG in sleep-related circadian problems in children with HIE.

关键字 Hypoxic-Ischemic encephalopathy (HIE); sleep problems; aEEG; circadian rhythmic issues; correlation

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Effects of transplantation of UC-MSCs and CB-MNCs on HIBD T lymphocytes in neonatal rats

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Objective
Human umbilical cord mesenchymal stem cells (UC-MSCs) and umbilical cord mesenchymal stem cells (CB-MNCs) were transplanted on newborn rats with hypooxic-ischemic brain damage (HIBD), the changes of regulatory T cells (Treg) in their spleen and peripheral blood were studied, and then their possible immune regulatory mechanisms were discussed and the immune regulatory capabilities of the two cells were compared.
Methods
1. Selected healthy 7-day-old neonatal SD rats and randomly divided them into UC-MSCs group, CB-MNCs group, HIBD group, and sham operation group. The HIBD model was prepared by Rice-Vannaucci method. The arteries were not subjected to ligation and shearing or ischemia and hypoxia.
2. Used enzyme digestion method to isolate UC-MSCs from human umbilical cord, flow cytometry to identify UC-MSCs surface antigen and Ficoll-Hypaque technology to separate CB-MNCs from cord blood.3. Injected 5μl of PBS, UC-MSCs (1 × 106 / cell) and CB-MNCs (1 × 107 /cell) into the HIBD group, UC-MSCs group, and CB-MNCs group respectively via the lateral ventricle 24h after modeling, and the sham operation group did not undergo injection treatment. The peripheral blood and spleen tissues of rats were taken 3 days, 5 days, 7 days and 14 days after injection, and lymphocytes in the spleen and peripheral blood were isolated. The CD4 + CD25 + Foxp3 + T cells (Treg cells) in peripheral blood and spleen were detected by flow cytometry and accounted for the proportion of lymphocytes to evaluate the effect of UC-MSCs and CB-MNCs transplantation therapy on the immune regulation of HIBD model in rats.
Results
1. In the spleen, the proportion of Treg cells to lymphocytes in the UC-MSCs transplantation group at 3, 5, sand 7 days after transplantation was higher than that in the HIBD group, but the difference was not statistically significant (P>0.05). The CB-MNCs transplantation group had a higher Treg ratio at 14 days than the HIBD group, and the difference was statistically significant (P<0.05). The proportion of Treg in UC-MSCs transplantation group at 3, 5, 7 and 14 days after transplantation was higher than that in CB-MNCs transplantation group, and the difference was statistically significant (P <0.05). Treg cells in the UC-MSCs transplantation group were higher than those in the sham operation group, and the difference was statistically significant (P<0.05). 2. The proportion of Treg cells in the cell transplantation group was higher than that in the sham operation group at 3, 5, 7 and 14 days after transplantation, and the difference was not statistically significant (P>0.05). 3. Compared with peripheral blood and spleen tissue, in the UC-MSCs transplantation group, Treg cells in peripheral blood were higher than those in spleen tissue at 3 days after transplantation, and the difference was statistically significant (P<0.05). The proportion of cells was higher than that in peripheral blood, and the difference was statistically significant (P<0.05).In the CB-MNCs transplantation group, the proportion of Treg cells in the spleen was lower than that in the peripheral blood, and the difference was not statistically significant (P>0.05). In the HIBD group, the proportion of Treg cells in the spleen decreased at 3, 7, and 14 days after transplantation compared with peripheral blood, and the difference was not statistically significant (P> 0.05).

Conclusions
1. One of the effective mechanisms of UC-MSCs and CB-MNCs transplantation in the treatment of HIBD may be to induce the proliferation of Treg cells, thereby playing the role of immunosuppression and reducing inflammation damage.2. Both UC-MSCs and CB-MNCs can play a role in inducing the proliferation and differentiation of Treg cells. UC-MSCs may regulate the differentiation and proliferation of Treg cells after transplantation may be earlier than CB-MNCs.

关键字 Umbilical cord mesenchymal stem cells; cord blood mononuclear cells

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Platelet Transfusion for Neonates with Thrombocytopenia: A Systematic Review and Meta-analysis

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ABSTRACT
Objective Thrombocytopenia is a common haemostatic abnormality with risks of bleeding and mortality among neonates. Platelet transfusion (PT) is a specific treatment for thrombocytopenia. To date, PT strategies (restrictive and liberal) are diverse as the relationship between PT and clinical outcomes is unclear. We proposed this systematic review and meta-analysis to collect and summarize current evidence concerning the PT strategy to reduce mortality, major bleeding, and morbidity among thrombocytopenic neonates.
Methods This systematic review was conducted according to the Cochrane Handbook for Systematic Review of Interventions and Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. A systematic search of the literature was performed in the PubMed, Cochrane Library, and Embase databases from database inception through January 5, 2021. The primary outcome was a combined outcome of mortality or major bleeding. We included RCTs and non-randomized studies enrolling preterm neonates (< 35 weeks) with thrombocytopenia (platelet counts <150×109/L) admitted to NICUs. The included studies should have two arms clearly comparing the two different platelet transfusion thresholds and should report at least one of the predefined clinical outcomes like mortality, major bleeding etc. Endnote X9 and Review Manager (RevMan) version 5.3 (Cochrane Collaboration, Oxford, UK) software were used to manage the selection process and statistical analysis, respectively. Two independent researchers performed the study selection, data extraction/coding, quality assessment and further analyses of the included studies, with disagreements being resolved by a third researcher.
Results We included three randomized controlled trials (RCTs) and one cohort study with a total of 1,144 neonates. A meta-analysis showed that restrictive PT tended to reduce events including mortality or major bleeding (n = 697, 2 RCTs, RR 0.76, 95% CI 0.57 - 1.02, random effects model; RR 0.74, 95% CI 0.57 - 0.96, fixed effect model) compared with liberal PT. There is no significant difference between restrictive and liberal PT on other morbidities (patent ductus arteriosus, bronchopulmonary dysplasia, sepsis, necrotizing enterocolitis, retinopathy of prematurity, coagulation disorders), and the length of stay.
Conclusion We found that restrictive PT strategies could reduce events including mortality and major bleeding. This provides support for the restrictive use of PT (therapeutic PT rather than prophylactic PT). It also highlights the need for more RCTs to explore the risks and overall benefits of PT, which will provide evidence for specific optimal thresholds for neonates with thrombocytopenia due to various pre-existing illness and more specific clinical features.

关键字 neonatal thrombocytopenia, platelet transfusion

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Placental disfunction: the core mechanism for poor neurodevelopmental outcome in offspring of maternal pre-eclampsia

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ABSTRACT

Objective Pre-eclampsia (PE) is leading disease threatening pregnant woman and their offspring. Offspring of PE pregnancies have high risk of poor neurodevelopmental outcomes and neuropsychological diseases in later life. However, the pathophysiological and pathogenesis remains undetermined. The abnormal placental functions are the core in most PE cases, and recent research evidence support that dysfunction of placenta may play an important role in prenatal brain development. Here, we suppose that PE disturb prenatal brain development through abnormal placental function. We summarize the possible mechanism of PE on neurodevelopmental outcomes in the offspring through the placental route.

Methods We searched in the PubMed, Cochrane Library, and Embase databases from database inception through April 5, 2021. Furthermore, we manually checked the references of all identified trials, relevant systematic reviews, and current treatment guidelines to avoid missing important studies. Missing data were handled by contacting relevant investigators for unreported materials or additional details.

Results Placental dysfunctions, like inadequate spiral arteries remodeling in PE causes dysregulated blood flow and consequently impaired maternal-placental-fetal material transport. Genetic and epigenetic variations relating metabolism of maternal hormone in PE disrupt special barrier of placenta. Reduced placenta-derived antiangiogenic factors, changed microbiota, alteration of synthetic function and immune disorders also contribute to the adverse effects of PE on neurodevelopmental outcomes in the offspring.

Conclusion Placenta as the interface between the mother and the fetus, provides nutrient and gas-waste exchange, hormone regulation, selective barrier to maintain pregnancy and support fetal development. Placental disfunction acts as the core mechanism for poor neurodevelopmental outcome in offspring of maternal pre-eclampsia.

关键字 prenaal brain development, pre-eclampsia, placental functions

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Association of neutrophil to lymphocyte ratio with preterm necrotizing enterocolitis: a retrospective case-control study

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Background: Necrotizing enterocolitis (NEC) is a leading cause of morbidity and mortality in premature. Few studies have investigated the relationship between the neutrophil to lymphocyte ratio (NLR) and NEC. We conducted a retrospective case-control study to investigate the relationship in preterm neonates.
Methods: A total of 199 preterm neonates diagnosed with NEC between January 2018 and January 2020 were included. For each preterm infant with NEC that graduated from the neonatal intensive care unit (NICU), preterm neonates who were not diagnosed with NEC (matched for gestational age and year of birth) were included as controls. Exclusion criteria were post-maturity, small or large for gestational age (week of pregnancy), congenital major anomalies, and cyanotic congenital heart disease. Univariate and multivariate logistic regression analyses were used to identify the association between NLR and preterm NEC.
Results: This study included 93 preterm neonates with NEC and 106 matched controls. There were no significant differences in gestational age (GA), birth weight (BW), age, sex, vaginal delivery (VD), chorioamnionitis (CA), and gestational diabetes mellitus (GDM) between the two groups. Compared with the control group, the lower and higher NLR levels in the NEC group were statistically different. Following univariate analysis, NLR was a risk factor for NEC (odds ratio [OR], 1.40; 95% confidence interval [CI], 1.00-1.90; P=0.042) and according to multivariate analysis, risk factors for NEC were NLR ≥3.20, and NLR <1.60, within 1 week before NEC diagnosis. There was a positive association between NLR and preterm NEC. Thus, NLR values of ≥1.60<3.20 were determined as the predictive cutoff values for protecting preterm from NEC (Model Ⅰ: OR, 0.20; 95% CI, 0.10-0.40; P<0.001) and (Model Ⅱ: OR, 0.10; 95% CI, 0.00-0.40; P<0.001].
Conclusions: NLR ≥1.60 and NLR <3.20 were associated with a decreased risk of NEC in preterm infants.

关键字 necrotizing enterocolitis, neutrophil to lymphocyte ratio, preterm neonates, diagnostic tools, predictive cutoff value

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Research about the effect of human milk fortifier on feeding intolerance of preterm infants and the other related factors

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Objective:
This study explores the effect of human milk fortifier (HMF) on the feeding intolerance (FI) of preterm infant, and provides a reference for the use of HMF in clinic. Furthermore, the other related factors of FI in preterm infants were explored, and we establish the FI prediction model to provide theoretical basis for preterm infants' early identification and treatment in clinical practice.
Methods:
Hospitalized premature infants in Neonatal Intensive Care Unit of West China Second University Hospital, Sichuan University, from June 2015 to November 2018, were retrospectively analyzed. Factors possibly related to premature infants' FI were recorded according to the detailed record of the patient's medical records:1.the history of pregnancy: gestational diabetes mellitus, prenatal use of glucocorticoids, placenta previa, placental abruption, fever in the third trimester;2. birth factors: birth weight, gestational age, sex, 1 minute Apgar score;3.postnatal factors: the time to feeding, the rate of adding milk, the use of HMF,the time to adding HMF, the initial dose of HMF, the rate of adding HMF, caffeine,respiratory support, pulmonary surfactant(PS), apnea,the duration of using antibiotic, blood transfusion, the time of blood transfusion, sepsis before FI, delay in meconium discharge, patent ductus arteriosus(PDA), dolichasigmoid; outcome: FI.
Results:
A total of 298 premature infants were included in the study,177(59.4%) cases were male,121(40.6%) cases were female, 650g≤birth weight ≤1980g, `x± s (1291.9 ± 249.2）g, 25w ≤ gestational age ≤ 36.6w, `x± s(30.0 ± 1.9） w; The multivariate analysis showed that there were no relationship between the use of HMF, the time to adding HMF, the initial dose of HMF with FI, but the rate of adding HMF was the risk factor of FI, otherwise, birth weight, nasal continuous positive airway pressure (NCPAP), the duration of using antibiotic were associated with FI, the birth weight was the protective factors. According to the rate of adding HMF, birth weight, respiratory support, the duration of using antibiotic, anemia, and time of blood transfusion, FI could be predicted in clinical work. The predictive model's AUC was 0.802, specificity is 0.75, sensitivity is 0.77, and accuracy is 0.76.
Conclusion:
1. HMF is not the risk factor of FI. While the increasing rate of HMF is the independent risk factor of FI. In preterm infants with gestational age less than 32w or birth weight less than 1500g, if the single milk volume is 30ml, adding 0.48-1.2g HMF daily can increase the risk of FI.
2. Birth weight was a protective factor of FI, while the NCPAP and the duration of using antibiotic were independence risk factors of FI, when the duration of using antibiotic is more than 2 weeks, the risk of FI can be markedly increased.
3. The rate of adding HMF, birth weight, respiratory support, the duration of using antibiotic, anemia, and the time of blood transfusion can be used to build prediction model, the AUC is 0.802, specificity is 0.75, sensitivity is 0.77, accuracy is 0.76.

关键字 Preterm infant; Feeding intolerance; Human milk fortifier; Risk factor; Prediction model

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Exploration of the training of Professional Pediatric Respiratory Therapists

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With the aggravation of sudden disease and emergency disasters in recent years at home, the critical care medicine and related medical technology are in progress and the occupation of respiratory therapist are gradually attracted people’s attention. The practitioner of respiratory therapy are trained professionally in various rescue and treatment instrument, therefore, they are competent of operating the instruments and clinical work. They are widely involved in the assessment, rescue and resuscitation of critical patients and health education in hospitals. Along with the perfectness and subdivision of respiratory treatment education system, the development of pediatrics and the increase of pediatric critical patients, the professional pediatric respiratory therapy practitioners in NICU and PICU emerge as the time requires, which plays a part in promoting the newborn and pediatric respiratory support and treatment technology gradually step to professional and standardized track. Take it as a starting by reviewing the pioneer of importing professional pediatric respiratory therapists in West China Second Hospital of Sichuan University, to explore and conclude in years of pediatric respiratory therapy,to analysis the present situation, and to combine the professional establishment mode of first batch of pediatric respiratory therapy in our hospital at home and the practical experience of pediatric respiratory therapy, it takes first step to explore the necessity, direction and strategy of pediatric respiratory therapists’ training. To sum up the experience, it is proved that the earliest professional pediatric respiratory therapists in China have played a positive role in pediatric specialty. They had helped reduce the mechanical ventilation related complications, improved the rescue treatment level and refined the professional division. They shows the importance and necessity of pediatric respiratory therapists. Pediatric respiratory therapy practitioners are relatively scarce, hence we actively advocate the sub-professional development of respiratory therapy, especially in the development of pediatrics.

关键字 Respiratory Therapy Practitioners, Respiratory Therapist, Pediatrics; Medical Service, Training Methods.

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Risk factors of death in congenital diaphragmatic hernia

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Abstract
Objective: To investigate the death risk factors of congenital diaphragmatic hernia.
Methods: the clinical data of children with congenital diaphragmatic hernia (CDH) from January 2017 to February 2021 in the Department of pediatric critical care medicine, Xinhua Hospital Affiliated to Shanghai Jiaotong University School of medicine were collected. The clinical data were retrospectively analyzed by case information system. According to the outcome, the children were divided into survival group and death group Birth style (cesarean section / natural labor), Apgar score (1 minute ≤ 7 points), transit time (time from delivery room to ward), location of diaphragmatic hernia (left / right), pulmonary artery pressure (the first cardiac ultrasound test after birth), oelhr (lung to head ratio), hospitalization days in pediatric intensive care unit (PICU) Arterial blood gas analysis indexes pH, lactic acid (LAC), OI [(PaO2 * map) / FiO2] within 1 hour after admission, PaO2 was arterial oxygen partial pressure, mPaw was mean airway pressure, FiO2 was percentage of inhaled oxygen concentration. The risk factors of death were analyzed by univariate and multivariate analysis.

Results: among 68 children, 42 (61.8%) were male and 26 (38.2%) were female; There were 54 cases (79.4%) with left diaphragmatic hernia and 14 cases (21.6%) with right diaphragmatic hernia; There were 23 cases in the death group, with a mortality rate of 33.8% (23 / 68); 14 cases died after operation, and the mortality rate was 23.7% (14 / 59); Univariate analysis showed that there were significant differences in gestational age, birth weight, Apgar score ≤ 7, PICU length of stay, oelhr, pulmonary artery pressure, pH and oi ($P < 0.05$). Multivariate logistic regression analysis showed that there were significant differences in pulmonary artery pressure, gestational age, birth weight, Apgar score ≤ 7, PICU length of stay and oi ($P < 0.05$).

Conclusion: the main risk factors of death in children with CDH include gestational age, birth weight, Apgar score ≤ 7, length of stay in PICU, pulmonary artery pressure, pH and oxygenation index (OI).

关键字 congenital diaphragmatic hernia, risk factors, causes of death

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The risk factors of severe hyperbilirubinemia due to ABO hemolytic disease of newborn and the timing of IVIG therapy

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Objective:
To analysis the risk factors of the severe hyperbilirubinemia associated with maternal-infant ABO blood incompability and the treatment opportunity of IVIG.
Materials and Methods:
We searched the digital databases of West China Second University Hospital. The excluding criteria including age ≥7 days, companied with other diseases (spesis, inherited metabolic disorders, congenital heart disease, coagulation disorders, intracranial hematoma, giant cephalhematoma et al), length of stay≤1 day, without complete medical records, gestational age≤35 weeks. Finally, a total of 948 newborns diagnosed with HDN were included in our study. We retrospectively collected the clinical features, including age, gender, level of bilirubin, therapy regimen, birth weight, time for phototherapy, laboratory test results et al. Then, all of the patients were divided into two groups, including pure phototherapy group (805 cases) and phototherapy plus IVIG group (143 cases). Decrease rates of bilirubin, decrease speed of bilirubin, related complications et al were analyzed.
Results:
1) In this study, 118 patients developed severe hyperbilirubinemia. The results of univariate Logistic regression analysis showed that gestational age≥37 weeks (OR= 3.44, 95%CI, 1.06-11.19), admission age> 24 hours, especially admission age> 48 hours (OR=48.34, 95%CI, 6.66-350.72), age>24 hours when jaundice was found (OR= 4.25, 95%CI, 2.54-7.13) are risk factors for severe hyperbilirubinemia in patients with ABO hemolysis disease. Multivariate logistic regression analysis showed: gestational age≤37weeks (OR= 4.19, 95%CI, 1.27-13.83), admission age>24 hours, especially admission age> 48 hours (OR=50.31, 95% CI, 6.93- 365.26) are risk factors for patients with ABO hemolytic disease.
2) In this study, there were 805 cases (84.92%) in the pure phototherapy group and 143 cases (15.08%) in the phototherapy plus IVIG group. There are no statistical difference between the pure phototherapy group and the phototherapy plus IVIG group in terms of average phototherapy time, average hospital stay, exchange rate, incidence of neonatal anemia, and incidence of bilirubin encephalopathy. Regression analysis showed that there was no statistical difference in the risk of re-admission between the two groups (P>0.05).
3) In the analysis with all the cases, we found that among HDN newborns with admission age ≤48 hours, the TSB decrease rates and descent speed in phototherapy plus IVIG group is higher than it in pure phototherapy group (P≤0.05), there are no significant differences in the average phototherapy time, average length of hospitalization, incidence of bilirubin encephalopathy, and readmission rate between the patients in the phototherapy plus IVIG group and the patients in the pure phototherapy group. For patients with admission age > 48hours, there is no significant difference between the phototherapy plus IVIG group and the pure phototherapy group in the bilirubin reduction rate, descent speed, average phototherapy time, average length of hospitalization, incidence of bilirubin encephalopathy, and readmission rate

Conclusion:
1) Gestational age ≥37weeks, admission age> 24 hours and age>24 hours when jaundice was found are risk factors of newborns with ABO-HDN developing severe hyperbilirubinemia.
2) For patients with ABO blood group incompatibility hemolytic disease whose admission age is less than 48 hours, phototherapy combined with IVIG therapy can effectively reduce the serum bilirubin level and avoid the occurrence of severe hyperbilirubinemia; for the patients whose admission age >48 hours, the use of IVIG can not reduce the length of hospitalization and phototherapy of the patients, and it does not help the reduction of bilirubin. Therefore, the use of IVIG is of little significance for children who are older than 48 hours at the time of admission.

关键字 Hemolytic disease of the fetus and newborn; Severe hyperbilirubinemia; Risk factors; Intravenous Immunoglobin G (IVIG)

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GROWTH AND NEURODEVELOPMENTAL OUTCOME AMONG PRETERM AND VLBW INFANTS GIVEN EARLY AGGRESSIVE AMINO ACID THERAPY ADMITTED AT THE NEONATAL INTENSIVE CARE UNIT OF UNIVERSITY OF SANTO TOMAS HOSPITAL

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Abstract Content Background and Relevance: Long-term outcomes of preterm and very low birth weight infants have been the focus of published research due to improved neonatal care. Long term morbidities associated with prematurity or VLBW is postnatal growth failure and neurodevelopmental delay. Different strategies were implemented including early aggressive amino acid therapy.

Objective: This study aims to determine growth and neurodevelopmental outcomes among preterm and VLBW infants given early aggressive amino acid therapy.

Methods All newborn infants who met the inclusion criteria admitted at the NICU were included in the study and started on parenteral nutrition containing amino acid at 3g/kg/day within 24 hours of life. Enteral feeding was initiated as soon as possible and tapering down of amino acids was started once patient can tolerate 70ml/kg/day of enteral feeds. The subjects' weight, length and head circumference was measured at birth and upon discharge and plotted against Fenton Chart. Once discharged, subjects were followed up at 6th, 9th and 12th month corrected age and assessed using the Bayley Scales of Infant and Toddler Development - Third Edition (BSID - III) Screening Tool for neurodevelopmental evaluation. Anthropometrics were measured and recorded and plotted in the WHO growth charts. Results gathered underwent statistical analysis, and if determined to have neurodevelopmental delay, an immediate referral to a neurodevelopmental specialist was done.

Results The patients were equally distributed in terms of gender and majority were classified as very preterm and very low birth infants with mean birth weight of 1.35 kg. The birth lengths were distributed at range interval of 30 and above with mean birth length of 40.6cm. The head circumferences had an average of 28.22cm. Most of the subjects stayed 15 to 40 days in the hospital with an average of 38.59 days.
The results showed that there were 12 (35.2%) participants below their normal weight from the target range of 10th to 90th percentile on the time of discharge with average weight of 1.98 kgs. At 6th month of corrected age, upon follow up, the number of participants with below normal weight decreased to 1 (2.94%) with average weight of 6.93 kgs. All participants had normal weight for age by 9th month of corrected age.
There were 7 (20.59%) participants with below normal linear length at the time of discharge with average length of 44.41 cm. By 6th month corrected age, it decreased to 3 (2.94%) with average weight of 65.42 cm, and by 9th month of corrected age, all participants had normal for age linear growth. As for head circumference, there were 4 (11.76%) participants with below normal head circumference at the time of discharge with average measure of 31.50 cm, and by 6th month of corrected age, all participants had normal measurement of head circumference.
The results showed that there were were 4 (13.8%) respondents classified as "emerging risk" while 25 (86.2%) subjects were classified as competent using Bayley scales on the 6th month. On 9th month of corrected age, only 2 (6.9%) were classified as "emerging risk" and it decreased to 1 (3.4%) by the 12th month of corrected age.

Conclusion Very preterm and very low birth weight infants are considered high risk population in developing long term complications related to prematurity such as problems in growth as well as neurodevelopmental delay. Early identification of such complications is important for prompt intervention. Results of this study clearly illustrates the long term benefits of giving early aggressive amino acid therapy among high risk neonates, specifically in terms of growth and neurodevelopment.However, one of the limitations of this study is the number of patients who were unable to complete the study. Also, the study, only followed up the participants up to 12 months of corrected age, and it would be better if they can be followed up until 2 years of age and longer. This research only focused on the nutritional intervention, in the form of early Amino Acid administration, and since neurodevelopmental delay can be multifactorial, another recommendation for future studies, is to include other factors that may influence the outcome of having neurodevelopmental delay such as episodes of hypoglycemia, sepsis etc.

Key words growth, neurodevelopment, outcome, preterm, very low birthweight, amino acid
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THE EFFECT OF ORAL VITAMIN E SUPPLEMENTATION IN DECREASING INCIDENCE OF RETINOPATHY OF PREMATURITY AMONG INFANTS <32 WEEKS AND <1500 GRAMS ADMITTED AT THE NEONATAL INTENSIVE CARE UNIT OF A TERTIARY HOSPITAL: A RANDOMIZED, DOUBLE BLINDED CONTROLLED TRIAL

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Abstract Content Background and Relevance: One of the major morbidities associated with prematurity is retinopathy of prematurity. With its progressive nature and debilitating complication, numerous studies have been published to prevent its increasing incidence. One of the proposed interventions is by giving antioxidants, specifically Vitamin E.

Objective: This study aims to determine if oral vitamin E supplementation can decrease the incidence of ROP among infants born <32 weeks or those weighing <1500 grams.

Methods All newborns who met the inclusion criteria admitted at the NICU will be randomly allocated into control (n=13) and treatment (n=13) group using a computer generated software. Those in the treatment group will receive oral supplementation of vitamin E to be given per OGT at 25 IU/day once a day to be started within 24 hours of life. The vitamin E will be administered with enteral milk feedings. Both groups will be screened by the same ophthalmologist on the day 20 of life and findings will be recorded using a standardized ROP screening form and incorporated in the chart. The subjects and the ophthalmologist who will screen the subjects are blinded to the study. Supplementation will be continued for at least 8 weeks OR until complete revascularization, whichever comes first, OR if with findings of severe retinopathy, until surgical intervention is warranted.

Results Results showed that the experimental group had a higher number of very preterm infants included in the study compared to control group (69.2% vs 46.2%). The control group on the other hand, had more patients classified as very low birth weight (53.8% vs 38.5%). Most of the patients were ventilated between 0 to 11 days in both groups, however, the experimental group had participants who had ventilatory support for 20 days and more. The number of patients who received blood transfusion were almost the same in both groups.

Of the 26 patients included in the study, 6 newborns (23%) were diagnosed to have ROP. From the control group, five out of 13 patients or 38.5% of the patients were diagnosed with retinopathy of prematurity, while 7.7% (1 out of 13) patients had retinopathy of prematurity in the experimental group. Comparatively, almost 30% was the percentage difference between two groups.

Stage 1 ROP was the most common finding occurring at 15.4% and 1 patient was also recorded to have Aggressive Posterior Retinopathy. In comparison to the experimental group which recorded 1 case of ROP Stage 1 and no cases of severe ROP.

The results show that there is only 7.7% probability of having sepsis and necrotizing enterocolitis among infants given Vitamin E supplementation similar to those who did not receive the supplementation.

The mean difference between two groups of the respondents' ROP was 0.308. The t-value of incidence of ROP was 1.922 with p-value equal of 0.067. The p-value between

two groups was more than 0.05. Thus, there was no significant difference between two groups in terms of incidence of ROP.

Conclusion Retinopathy of prematurity remains to be one of the morbidities associated with prematurity as survival rate among preterm newborns improve. Because of the progressive nature of this condition, researches have been done to find ways to prevent this disease, and one of the strategies looked into is by use of Vitamin E as an antioxidant.

While the results of this study do not seem to support significance in decreasing incidence in ROP among high risk neonates, this study then provides new insight in the possibility of preventing severe forms of ROP. This is in line with published prospective cohort study wherein a 50% reduction in severe ROP was documented. This study also clearly illustrated the safe use of oral vitamin E, without increased risk in neonatal sepsis and necrotizing enterocolitis.

To better understand the possible benefits of this intervention, future studies could be done, making use of larger sample size with each group (VLBW, ELBW, very preterm, and extremely preterm infants) better represented to determine statistical significance of this strategy.

Key words Vitamin E, Retinopathy of prematurity, antioxidant

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A case of neonatal ornithine carbamoyltransferase deficiency and discussion

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Objective: To improve the understanding of the clinical and genetic characteristics of neonatal ornithine carbamyltransferase deficiency (OTCD), and to investigate the outcome of neonatal OTCD.

Methods: The clinical data of 1 child with OTCD admitted to the neonatal Department of Jiangxi Children's Hospital in November 2017 were summarized. The clinical characteristics, laboratory examination, genetic results, autopsy report, treatment and outcome of the disease were retrospectively analyzed.

Results: The main clinical manifestations were consciousness disturbance, vomiting, convulsion and so on. The auxiliary examination found increased blood ammonia, decreased citrulline, increased urinary whey acid, and signs of cerebral edema on cranial imaging. Ornithine aminotransferase (OTC) gene was detected to cause the mutation. After active treatment, the child died at 56 days of age. Conclusion: OTCD is mainly manifested as central nervous system dysfunction caused by hyperammonemia, and the peak concentration of blood ammonia is closely related to the prognosis of patients' neurological function. Therefore, children with unknown vomiting and consciousness disorders should be highly alert to the possibility of OTCD, and OTCD patients with neonatal onset often have poor prognosis.

关键字 鸟氨酸氨甲酰转移酶缺乏症；新生儿；高氨血症

分类：16. Neonatology 新生儿
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Analysis of neonatal diseases caused by exon7 mutation of HNF4A gene

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Objective: To investigate the clinical characteristics of neonatal hypoglycemia, hyperlactate and hyperammonemia caused by exon7 mutation of HNF4A gene. Methods: the data of neonatal girls, HNF4A gene analysis and follow-up were analyzed, and the relevant literature was reviewed. Taking "HNF4A", "chr20:43048381" and "neogenetic hyperglycemia" as the search words, we consulted the online human Mendelian genetic database, PubMed database, China HowNet database and Wanfang database respectively, and summarized the clinical manifestations, laboratory and imaging examination, treatment and prognosis of children with exon7 mutation of HNF4A gene. Conclusion: most of the manifestations of neonatal hypoglycemia will affect the development of cerebral cortex, and seriously affect the body metabolism and life-threatening. However, recurrent hypoglycemia with hyperlactatemia and high blood ammonia rise are rare. This case was diagnosed by gene analysis. At present, there is no clear treatment method. Most of them are treated by emergency treatment of hypoglycemia, anti infection and improving children's nutrition. After the hypoglycemia was controlled by improving the nutritional heat card of the child, the child did not have hypoglycemia again. After the full course of short periodic antibiotics, the blood ammonia value of the child decreased, and the clinical symptoms were improved. Since the child is still in the neonatal period, no other special treatment has been carried out, and regular follow-up is still ongoing.

关键字 Neonatal hypoglycemia; Hyperammonemia; gene diagnosis

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Serum insulin、IGF－1 and growth hormone in intrauterine growth restriction infants

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Abstract: Objective To study the relationship between the occurrence of intrauterine growth retardation (IUGR) and postnatal blood insulin, insulin-like growth factor-1 and growth hormone, and to explore the characteristics of endocrine environment of newborns with IUGR. Methods The children with IUGR diagnosed in the neonatal department of our hospital from June 2019 to August 2021 were selected as the experimental group, and the full-term children of appropriate age admitted in the same time period were selected as the control group. In IUGR group, there were 30 cases on the 1st day, 30 cases on the 7th day, 20 cases on the 21st day and 30 cases in the control group. The changes of insulin, IGF-1 and growth hormone in IUGR group and control group were measured and compared on the first, seventh and 21st day after birth. Results ① The level of serum IGF-1 in IUGR group was significantly higher than that in control group on the first day after birth ($P < 0.05$). ② On the 7th day after birth, the levels of serum IGF-1 and growth hormone in IUGR group were significantly higher than those in control group ($P < 0.05$). ③ On the 21st day after birth, the level of blood growth hormone in IUGR group was significantly higher than that in the control group ($P < 0.05$). Conclusions The growth and development of IUGR newborns are regulated by endocrine environment. The early stage of IUGR newborns is catch-up growth, and the negative feedback secretion increases the levels of IGF-1 and growth hormone.

关键字 Intrauterine growth retardation; Insulin; Insulin－like growth factor-1;Growth hormone;Neonata

Category: 16. Neonatology 新生儿
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The Mechanism of Caffeine Activate the Neurons of Medial Parabrachial Nucleus to Reduce the Apnea Neonatorum

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Abstract Content Objective: To investigate the effect and mechanism of caffeine in MPB (Medial parabrachial nucleus) of mice in different ages and provide a reference to investigating new drugs on specific target.

Methods Healthy C57BL/6 mice in 4 age groups were used in our experiments. The mice with the age < 22 d were divided into newborn group; the mice with age between 22 and 30 d were divided into junior group; the age 31~60 d in young group and the age > 60 d in adult group. During firing recording, different drugs were applied to investigate the mechanism of caffeine, including caffeine, CPT and KW6002. The dimethyl sulphoxide (DMSO) was used as a solvent of CPT and KW6002. And the locus ceruleus (LC) was used as a contrast of MPB. The picrotoxinin (PTX) was performing a role of antagonist of GABAA receptors while the NBQX and APV as antagonist of glutamate receptors. Thus the spontaneous excitatory/inhibitory postsynaptic currents (sEPSC/sIPSC) can be detective. The tetrodotoxin (TTX) was also adopted to block the Na+ channels in order to eliminate the action-potential-depended currents. The firing rates, the rates as well as amplitudes of sEPSC and sIPSC were recorded and analyzed as a parameter of activation and depression. Since not all cells in MPB have spontaneous action potential, those not were holded in a condition of firing rate between 1-10 to better see the effects of drugs.

Results (1) Electrophysiological property and the differences of MPB neurons among groups: Totally 219 cells were patched. 64 were in newborn group, 62 in junior group,65 in young group and 28 in adult group.
Significant differences were found in the membrane capacitance (Cm) between groups of newborn-young, newborn-adult,junior-young, as well as junior-adult ($P < 0.05$). The spontaneous firing rates were different between newborn and junior group ($P = 0.002$). The membrane potential,input resistance, hyperpolarization-activated (Ih) currents and low-threshold spiking (LTS) had no significant difference between groups ($P > 0.05$).
(2) Excitive effect of caffeine in MPB neurons: Neurons in good condition were involved in this part. Totally 28 neurons were tested with no exogenous adenosine applying. Among which 9 neurons were in newborn group, 5 in junior group, 6 in young group and 8 in adult group. The number of excited neuron was 21 in total with excitable proportion of 75%. And 8 of them were in newborn group, the excitable proportion of newborn group was 88.89%. Junior group owned 4 excitable neurons(80.0%); and 5 in young group (83.33%); 4 in adult group (50%). No significant difference was found between all group ($P = 0.275$). For comparing, 6 neurons in locus ceruleus (LC) were tested with excitable neurons only 1 (16.67%). The excitable proportion was found significantly different between MPB and LC neurons($P = 0.014$).
(3) Using CPT and KW6002 to mimic the effect of caffeine in MPB: Totally 12 cells were tested with CPT. Among them 9 cells could be excited. The proportion of excited cells was 75%. Using KW6002 to replace CPT could excite 1 of 8 MPB neurons. The proportion of excited cells was 12.5%. DMSO group was set to be a vehicle control

group with the concentration of DMSO of 0.02‰. The excitable proportion of CPT and caffeine had no significant difference (P > 0.05); The excitable proportion of KW6002 and caffeine were significantly different (P <0.05). The DMSO had no effect on MPB neurons.
(4) The effect of Caffeine in MPB with TTX: 1 μmol TTX could completely eliminate the spontaneous action potential. Totally 3 neurons were tested and the caffeine could not excite MPB neurons in the existent of TTX. The excitable proportion turned into 0.The membrane potential had no significant difference before and after caffeine’s applying (P > 0.05).
(5) sEPSC and sIPSC: Caffeine could increase the frequency and the amplitude of sEPSC in the existent of PTX. The frequency had significant difference before and after applying of caffeine (P<0.05). While Caffeine could not decrease the frequency or amplitude of sIPSC (P > 0.05).
Conclusion 1. Caffeine can specifically excite the MPB neurons of mice despite different ages.
2. Caffeine may excite MPB neurons by blocking A1 receptors.
3. Caffeine can increase the efficiency of synaptic transmission of MPB.

Key words Caffeine; MPB; Apnea Neonatorum; Adenosine A1 Receptor
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Urinary Organophosphate Metabolite Concentrations and Birth Outcomes among Women Conceiving through in Vitro Fertilization in Shanghai, China

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Background: Some legacy and emerging environmental pesticide contaminations are suspected risk factors for intrauterine growth restriction. However, few studies have examined the adverse birth outcomes of preconception exposure to organophosphate pesticides (OPs), a widely used class of pesticides, in women undergoing in vitro fertilization (IVF).
Objectives: We investigated the relationship of preconception OP exposure with birth outcomes among women undergoing IVF in a Chinese population.
Methods: This study included 302 couples seeking infertility treatment in the China National Birth Cohort (CNBC) Study, Shanghai, China, who gave birth to 302 singleton infants between 2018 and 2021. Demographic and clinical information were collected from medical records and through questionnaires. We measured the concentrations of six nonspecific DAP metabolites of OPs [diethylthiophosphate (DETP), diethylphosphate (DEP), diethyldithiophosphate (DEDTP), dimethyldithiophosphate (DMTP), dimethylphosphate (DMP), dimethyldithiophosphate (DMDTP)] in maternal spot urine samples collected at recruitment. Generalized linear models (GLMs) and weighted quantile sum (WQS) regression analyses were performed to examine the associations of individual and joint effects of exposure to OPs with birth outcomes, respectively. Odder ratios (OR) of preterm birth (< 37 weeks gestation) were estimated using binary logistic regression models.
Results: Women in the highest as compared with lowest quartile of DEP had shorter gestational age. The association was modified by gender, with boys showing larger decreases in gestational age. Results from linear models with individual DAP metabolites were corroborated by the WQS regression where DEP had the largest contribution to the overall mixture effect on gestational age. Moreover, the highest versus lowest quartile of DEP was associated with an elevated risk of preterm birth.
Conclusion: Preconception OP exposure in particular individual DEP was associated with shortened gestational age, and the association was more pronounced among boys.

关键字 organophosphate pesticide; in vitro fertilization; birth outcomes; preterm birth; China

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a case of type craniosynostosis syndrome

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Abstract: a case of type craniosynostosis syndrome women 27 minutes, clinical manifestations of craniosynostosis, skull is absent, facial hypoplasia, eyes malformation, born after merging difficulty breathing, shortness of breath and inspiratory three concave), on the basis of clinical data and imaging findings, clinical diagnosis of craniofacial LuZong syndrome type

关键字 克鲁宗综合征 散发型 颅面畸形

分类：16. Neonatology 新生儿
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Effect of Probenecid on Endothelial Cell Growth Rate and Retinal Angiogenesis in Oxygen-Induced Retinopathy model

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Objectives: Probenecid is an anion transport inhibitor, which, according to the connectivity map (CMap; a biological application database), interferes with hypoxia-induced gene expression changes in retinal vascular endothelial cells (ECs). Here, we investigated the influence of probenecid on retinal ECs cytotoxicity and retinal neovascularization in a murine oxygen-induced retinopathy (OIR) model. Methods: Retinal ECsgrowth rate in the presence of hypoxia-mimicking concentrations of cobalt chloride (CoCl2) was determined using the thiazolyl blue tetrazolium bromide (MTT) assayandproliferating cell nuclear antigen (PCNA) expression. In OIR rats, probenecid was administered by intraperitoneal injection (i. p.) from postnatal day (P) 1 to P7. The concentrations of vitreous humor vascular endothelial growth factor (VEGF), hypoxia-inducible factor (HIF)-1α, and placental growth factor (PlGF) were determined by ELISA at P21. The amount of newly formed vascular lumen was evaluated by histopathological examination. Retinopathy and neovascularization were assessed by scoring isolectin B4 fluorescein-stained retinal flat mounts. Western blots for liver tissue HIF-1α and hepcidin (HAMP) were performed. Results: In vitro, probenecid led to the recession of hypoxia-induced ECgrowth rateproliferation. In vivo, compared to the controlOIR retina, upregulation of VEGF, HIF-1α, and PlGF in phase II retinopathy of prematurity (ROP) was inhibited by probenecid administration. Moreover, probenecid ameliorated neovascularization and resulted in significantly reduced relative leakage fluorescence signal intensity in fluorescence-stained retinal flat mounts ($P < 0.05$). Probenecid alleviatedsuppressedthe liver overactivation of HIF-1α andHAMP anddownregulation of HIF-1α in the OIR modelrats. Conclusions: This is the first demonstration that probenecid may be a protective compound against retinal angiogenesis in OIR. These changesareaccompanied withdecreased hyperoxia-mediated hepcidinoverproduction.Although the relevance of the results to ROP needs further research, these findings may help to establish potential pharmacological targets based on the CMap database.

关键字 CMap， retinopathy of prematurity， probenecid, vascularization, hepcidin
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The Effect of PDSA Quality Improvement Model on Breastfeeding Rate of Late Preterm Infants during hospitalization

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Objectives To assess the effect of PDSA quality improvement model on breastfeeding rate of late preterm infants during hospitalization. Methods Analysis was performed for the clinical data of late preterm infants who were admitted from March to December 2018(non-quality improvement group, NQI group) and those who were admitted from January to October 2019 after the implementation of quality improvement measures(quality improvement group, QI group). The parameters including the situation of breastfeeding (breastfeeding rate and breastfeeding amount), the growth rate of body weight, the duration of parenteral nutrition and the incidence of feeding intolerance. Results Compared with the NQI group, the breastfeeding rate and amount and the growth rate of body weight were significantly increased, while the duration of parenteral nutrition and the incidence of feeding intolerance were significantly decreased. Conclusions The PDSA quality improvement model can increase breastfeeding rate of late preterm infants and decrease gastrointestinal complications in late preterm infants.

关键字 Quality improvement, Late preterm infants, Breastfeeding

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The Effect of Different Breastfeeding Rate on the Development of Infection-related Diseases in Late Preterm Infants during hospitalization

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Objectives To assess the incidence rate of infectious diseases in late preterm infants during hospitalization, explore the factors for infectious diseases and the effect of breastfeeding on the development of infectious diseases. Methods This study retrospectively analyzed the clinical data of late preterm infants who were admitted from January 2018 to December 2019. Based on the feeding pattern, they were divided into three groups. Differences were compared in terms of general status and the incidence of infectious diseases. Factors for infectious diseases were investigated using univariate and multivariate logistic regression analysis. Results A total of 396 late preterm infants were enrolled, and they were divided into 3 groups: breastfeeding ≥50% group (n=98), breastfeeding <50% group (n=102) and the formula feeding group (n=196). Totally the incidence rate of infectious diseases was 12.63%(50/396), with the incidence rate of infectious diseases in the breastfeeding ≥50% group and the breastfeeding <50% group were significantly lower than the formula feeding group(6.1% vs 6.9% vs 18.8%, P=0.036). Multivariate logistic regression analysis showed that breastfeeding was a protective factor against infectious diseases(OR=0.547, P=0.021), while male sex, the smaller the gestational age, invasive ventilation and central vein catheterization were risk factors for infectious diseases (OR=1.626, 11.703 and 8.262 respectively, P<0.05). Conclusions In late preterm infants, breastfeeding could significantly reduce the incidence rate of infectious diseases and is an independent protective factor against infectious diseases. We should actively promote the breastfeeding rate for late preterm infants during hospitalization.

关键字 Breastfeeding, Late preterm infants, infection.

分类：16. Neonatology 新生儿
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Early vitamin A supplementation for prevention of short-term morbidity and mortality in very-low-birth-weight infants: a systematic review and meta-analysis

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Background: Vitamin A plays an important role in the development and maintenance of the normal function of organs and systems. Premature infants have low levels of vitamin A, which may be associated with an increased risk of developing disease. This study aimed to evaluate the effects of vitamin A supplementation on short-term morbidity and mortality in very-low-birth-weight (VLBW) infants.
Methods: We used PubMed, EMBASE, the Cochrane Central Register of Controlled Trials, and Web of Science to conduct a literature search of studies published before June 1, 2021, to be included in our meta-analysis. The analysis included randomised controlled trials that compared the effects of vitamin A supplementation on VLBW infants (birth weight ≤ 1500 g) and controls given a placebo or no treatment. The data were independently screened, extracted, and assessed for risk of bias by two reviewers. The findings are presented as risk ratios and mean differences (MD) within 95% confidence intervals (CI).
Results: Twelve randomised controlled trials were included in the meta-analysis, and 2,111 infants were pooled and analysed. Compared with the control group, vitamin A supplementation reduced the length of hospital stay (MD: -12.67, 95% CI: -23.55 to -1.79). Additionally, the plasma retinol levels were significantly higher in the vitamin A group than in the control group (MD, 24.74; 95% CI: 6.62 - 42.87). The incidence of periventricular leukomalacia and retinopathy of prematurity of any grade was also significantly different between the two groups. However, there was no reduction in the risk of oxygen requirement at 28 days or 36 weeks' postmenstrual age (PMA) and death before 1 month or at 36 weeks' PMA. There was also no reduction in the risk of intraventricular haemorrhage, retinopathy of prematurity requiring treatment, necrotising enterocolitis, or sepsis.
Conclusions: There is no sufficient evidence regarding vitamin A supplementation preventing bronchopulmonary dysplasia in VLBW infants. Vitamin A supplementation can reduce the incidence of retinopathy of prematurity of any grade, reduce duration of hospital stay, and may exert an effect of preventing periventricular leukomalacia.

关键字 Vitamin A, Very-low-birth-weight, Meta-analysis

分类：16. Neonatology 新生儿
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Atorvastatin for attenuating neuronal apoptosis in hypoxic-ischemic neonatal rats

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Background: Neuronal apoptosis is one of the main pathological processes of hypoxic-ischemic brain damage (HIBD) and is involved in the development of hypoxic-ischemic encephalopathy (HIE) in neonates. Atorvastatin has been found to have neuroprotective effects in some nervous system diseases, but its role in regulating the pathogenesis of neonatal HIBD remains elusive. Thus, this study aimed to explore the effects and related mechanisms of atorvastatin on the regulation of neuronal apoptosis after HIBD in newborn rats.
Methods: The rat HIBD model and the neuronal oxygen glucose deprivation (OGD) model were established routinely. Atorvastatin, AC inhibitor (SQ22536) and BDNF inhibitor (ANA-12) were used to treat HIBD rats and OGD neurons. Cerebral infarction, learning and memory ability, cAMP/PKA/p-CREB/BDNF signaling molecules, and apoptosis-related indicators (TUNEL, cleaved caspase-3, and Bax/Bcl2) were then examined.
Results: Atorvastatin reduced cerebral infarction, improved learning and memory ability, decreased the number of TUNEL-positive neurons, inhibited the expression of cleaved caspase-3 and Bax/Bcl2, and activated the cAMP/PKA/p-CREB/BDNF pathway in the cerebral cortex after HIBD. It also decreased the number of TUNEL-positive neurons, inhibited the expression of cleaved caspase-3 and Bax/Bcl2, and activated the cAMP/PKA/p-CREB/BDNF pathway in neurons after OGD. Furthermore, inhibition of cAMP or BDNF attenuated the effect of atorvastatin on the inhibition of neuronal apoptosis.
Conclusions: Atorvastatin inhibits HIBD-induced neuronal apoptosis and alleviates brain injury in neonatal rats, mainly by activating the cAMP/PKA/p-CREB/BDNF pathway. Thus, atorvastatin may be developed as a potential drug for the treatment of neonatal HIE.

关键字 Hypoxic ischemic; Neuron; Apoptosis; cAMP/PKA/p-CREB/BDNF pathway

分类：16. Neonatology 新生儿
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Clinical effect of NAVA combined with PS in the treatment of neonatal respiratory distress syndrome and its effect on prognosis

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[Abstract] Objective: To explore the clinical efficacy of NAVA combined with PS in the treatment of neonatal respiratory distress syndrome and its effect on prognosis. Methods: According to 44 cases of neonatal respiratory distress syndrome treated from June 2017 to October 2018, they were divided into control group (n = 22) and observation group (n = 22) according to length of stay. The control group was given NAVA treatment, and the observation group was combined with PS treatment on the basis of the control group. The patient's effect was evaluated after treatment, and the clinical treatment effect, blood gas level recovery and incidence of adverse reactions were compared between the two groups. Results: After comparing the treatment effects of neonates in the two groups in terms of length of stay, apnea episodes, and ventilator use, the treatment effects of the observation group were significantly better than those of the control group (P <0.05). The recovery of blood gas level was significantly better than before treatment. The children's vital capacity, expiratory flow rate, and blood oxygen saturation levels in the observation group were better than those in the control group (P <0.05). According to the adverse reactions of the two groups of children, there were: Electrolyte disorders, irritability, tachycardia, feeding intolerance, etc. The adverse reaction rate in the observation group was 22.72%, and the adverse reaction rate in the control group was 45.45%. The adverse reaction rate in the observation group was significantly lower than that in the control group (P <0.05). Conclusion: The clinical efficacy of NAVA combined with PS in the treatment of neonatal respiratory distress syndrome is significant, which is conducive to improving the vital capacity and blood gas recovery of neonates, reducing the occurrence of adverse events and length of hospital stay. It is worth popularizing and applying.

关键字 NAVA; PS treatment; newborn; respiratory distress syndrome; clinical efficacy; prognosis

分类：16. Neonatology 新生儿
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Intensive phototherapy versus exchange transfusion for the treatment of neonatal hyperbilirubinemia: a multicenter retrospective cohort study

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Abstract

Background

Intensive phototherapy (IPT) and exchange transfusion (ET) are the main treatments for extreme hyperbilirubinemia. However, there is no reliable evidence on determining the thresholds for these treatments. This multicenter study compared the effectiveness and complications of IPT and ET in the treatment of extreme hyperbilirubinemia.

Methods

This retrospective cohort study was conducted in seven centers from January 2015 to January 2018. Patients with extreme hyperbilirubinemia that met the criteria of ET were included. Patients were divided into three subgroups (low, medium, and high risk) according to gestational week and risk factors. Propensity score matching (PSM) was performed to balance the data before treatment. Study outcomes included the development of bilirubin encephalopathy, duration of hospitalization, expenses, and complications. Mortality, auditory complications, seizures, enamel dysplasia, ocular motility disorders, athetosis, motor, and language development were evaluated during follow-up at age 3 years.

Results

A total of 1,164 patients were included in this study. After PSM, 296 patients in the IPT only group and 296 patients in the IPT plus ET group were further divided into the low-, medium-, and high-risk subgroups with 188, 364, and 40 matched patients, respectively. No significant differences were found between the IPT only and IPT plus ET groups in terms of morbidity, complications, and sequelae. Hospitalization duration and expenses were lower in the low- and medium-risk subgroups in the IPT only group.

Conclusions

Our results suggest that the ET threshold should be increased. Accordingly, ET for patients with hyperbilirubinemia could be reduced. Complications of ET could be reduced, and blood products could be saved.

关键字 Intensive phototherapy; exchange transfusion; neonatal hyperbilirubinemia

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Research progress of follow-up compliance of premature infants after discharge

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To summarize and analyze the status quo and influencing factors of the follow-up compliance of premature infants after they have been discharged from the NICU, and put forward relevant suggestions to provide a reference for enhancing the follow-up compliance of premature infants.

关键字 Infant,Premature; Follow up; Compliance;

分类：16. Neonatology 新生儿
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An evidence-based sustained quality improvement initiative to reduce invasive fungal infection in a neonatal intensive care unit

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Objective To study the effect of an evidence-based sustained quality improvement initiative for reducing invasive fungal infection (IFI) in a neonatal intensive care unit (NICU).
Methods The study retrospectively included all infants admitted to our NICU during the before-after quality improvement from September, 2015 to August, 2018, and was conducted in 3 phases: the baseline phase (September, 2015-August, 2016), the invention phase (September, 2016-August, 2017) and the sustained quality improvement phase (September, 2017-August, 2018). Outcome measures were IFI rates and central line (CL) associated bloodstream fungal infection rates in the 3 phases. Process measures were antibiotic use rates (defined by dividing antibiotic days by total patients days *100%) and CL utilization ratios (defined by dividing CL days by total patient days among patients with CL). Chi-square test, one-way ANOVA, multivariate logistic regression, Poisson regression and statistical process control charts were used for statistical analysis.
Results A total of 4728 infants were included in the study. 14 infants developed IFI corresponding to 3.0 per 1000 patients. The IFI rate decreased to 0.7 per 1000 patients in the sustained quality improvement phase compared with 4.8 per 1000 patients in the baseline phase by multivariate logistic regression (OR=0.11, 95%CI: 0.01-0.85, P=0.034). The CL associated bloodstream fungal infection rates were 1.1 per 1000 CL days in the baseline phase, 0.5 per 1000 CL days in the intervention phase and 0.1 per 1000 CL days in the sustained quality improvement phase, and decreased significantly by Poisson regression (IRR=0.40, 95% CI: 0.17-0.94, P=0.035), with the CL utilization ratios of 0.45, 0.47 and 0.42, respectively. The antibiotic use rates decreased from 67.8% in the baseline phase, to 58.0% in the intervention phase to 49.8% in the sustained quality improvement phase.
Conclusions The evidence-based sustained quality improvement initiative is effective in reducing IFI and CL associated bloodstream fungal infection in the neonatal intensive care unit.

关键字 Invasive fungal infection; Neonatal intensive care unit; Quality improvement
分类：16. Neonatology 新生儿
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CYP2C9*3 increases the ibuprofen response in hemodynamically significant patent ductus arteriosus infants with gestational age more than 30 weeks

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Abstract
Background
Hemodynamically significant patent ductus arteriosus (hsPDA) is a severe condition in newborns. Ibuprofen is effective treatment to reduce the severe complications and the need for surgical treatment. Several single nucleotide polymorphisms (SNPs) were related to the ibuprofen metabolism, treatment effects and the rate of side effects. The effects of SNPs to hsPDA response after ibuprofen treatment is unknown.
Method
We recruited hsPDA patients with standard ibuprofen treatment. Those patients had participated in China Neonatal Genomes Project (CNGP, ClinicalTrials.gov Identifier: NCT03931707) with next generation sequencing data. We reanalyzed the sequencing data and compared the alleles frequencies of known ibuprofen related SNPs between ibuprofen Responder and Non-responder groups.
Results
In total, 185 hsPDA patients were recruited with gestational age (GA) ranging from 24 to 40 weeks. No significant differences were detected in basic information, period of ibuprofen treatment, rate of conservative treatment, complications and side effects between ibuprofen Responder group and Non-responder group. Seventeen hsPDA carried CYP2C9*3 and 1 with CYP2C9*2 were detected. In GA>30 wks group, we found higher allele frequency of CYP2C9*3 in Responder group than in Non-responder group (16% vs 0, P=0.0391). In GA≤30 wks group, the sum allele frequency of CYP2C9*3 and CYP2C9*2 had no difference between two groups (Responder group vs Non-responder group, 13% vs 11%, P=0.768).
Conclusion
For hsPDA patients with gestational age more than 30 weeks, genetic tests of CYP2C9*3 site may benefit the prediction of ibuprofen treatment outcome.

关键字 patent ductus arteriosus, neonatology, CYP2C9

分类：16. Neonatology 新生儿
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Effects of IGF-1, leptin, and ghrelin on protein-to-energy ratio intake and body composition of very preterm infants: a mediation analysis

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Objectives: To investigate the relations between early protein intake, serum hormones, and body composition at term age in very preterm infants.
Methods: Fifty-eight very preterm infants were included in the cohort study. Average value of daily protein-to-energy (P/E) ratio intake for enteral and parenteral nutrition (EN and PN) across the first 28 days were collected. Levels of IGF-1, leptin, and ghrelin, and body composition were evaluated at term age. Multiple linear regression analysis is used to detect the relations between P/E ratio intake, serum hormones, and body composition. Bootstrapping tests are used to verify mediation effects of serum hormones between P/E ratio intake and body composition.
Results: P/E ratio for EN had positive associations with body weight z-score (β=0.42, 95% CI 0.13, 0.71), fat mass (FM, β=0.91, 95%CI 0.30, 1.53), percentage of body fat (PBF, β=1.10, 95%CI 0.43, 1.77), IGF-1 (β=12.77, 95%CI 2.08, 23.46) and leptin (β=6.76, 95%CI 2.99, 10.53) at term age. P/E ratio for PN had negative relation with z-score of PBF (β=0.35, 95%CI -0.67, -0.03) and leptin level (β=1.58, 95%CI -2.50, -0.66). Higher level of IGF-1 and leptin was associated with higher body weight and body fat at term age (all P-values <0.05). But higher ghrelin level was associated with lower body weight and body fat. IGF-1 and leptin mediated the relations between P/E ratio for EN and body weight and body fat. Leptin has a mediation effect between P/E ratio for PN and PBF at term age.
Conclusion: Parenteral and enteral protein intake have different effects on serum hormones. IGF-1 and leptin have mediation effects between the relations of protein intake and body composition.

关键字 neonate; IGF-1; leptin; ghrelin; body composition

分类：16. Neonatology 新生儿
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A Modified Lung Ultrasound Score to Predict Short-Term Clinical Outcomes of Bronchopulmonary Dysplasia

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Background: Lung ultrasound (LUS) is a useful tool for assessing the severity of lung disease, without radiation exposure. However, there is little data on the practicality of LUS in assessing the severity of bronchopulmonary dysplasia (BPD) and predicting short-term clinical outcomes. We make a modified LUS score to evaluate BPD severity and assess the reliability of mLUS score in predicting short-term clinical outcomes.
Methods: Prospective diagnostic accuracy study was designed to enroll preterm infants with gestational age < 34 weeks. Lung ultrasonography was performed at 36 weeks postmenstrual age. The diagnostic and predictive values of new modified lung ultrasound (mLUS) scores based on eight standard sections were compared with classic lung ultrasound (cLUS) scores.
Results: A total of 128 infants were enrolled in this cohort, including 30 without BPD; 31 with mild BPD; 23 with moderate BPD and 44 with severe BPD. The mLUS score was significantly correlated with the short-term clinical outcomes, superior to cLUS score. The mLUS score well predicted moderate and severe BPD (AUC = 0.813, 95% CI: 0.739-0.888) and severe BPD (AUC = 0.801, 95% CI: 0.728-0.875), which were superior to cLUS score. The ROC analysis of mLUS score to predict the other short-term outcomes also showed significant superiority to cLUS score. The optimal cutoff points for mLUS score were 14 for moderate and severe BPD and 16 for severe BPD.
Conclusions: The mLUS score correlates significantly with short-term clinical outcomes and well predicts these outcomes in preterm infants.

关键字 Lung ultrasound, bronchopulmonary dysplasia, premature

分类：16. Neonatology 新生儿
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Fitness of INTERGROWTH-21st birthweight standard for Chinese babies

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Objective. To determine the fitness of the INTERGROWTH-21st birth weight standard for Hong Kong babies compared to the local reference.
Methods. Live births in Hong Kong's public hospitals from 1/1/2006 to 13/12/2017 were included if born between 24 and 42 complete weeks' gestation. Babies' birth weight Z-scores were calculated using published methods for the local and the INTERGROWTH-21st references. The two references were compared in three aspects: 1) the proportions of large- or small-for-gestational-age (SGA) infants, 2) the gestation- and sex-specific mean birth weight Z-scores, and 3) the predictive power for SGA related complications, including intrauterine growth restriction, hypoglycemia, hypothermia, polycythemia, thrombocytopenia, and neutropenia.
Results. A total of 488,896 infants were included. Using the INTERGROWTH-21st standard, among neonates born <33 weeks' gestation, the mean birth weight Z-scores were close to zero (-0.2 to 0.05), while they were away from zero (0.06 to 0.34) after excluding high-risk infants. Compared to the local reference, the INTERGROWTH-21st standard classified smaller proportions of infants as SGA (8.3% vs. 9.6%) and LGA (6.6% vs. 7.9%), especially SGA among preterm infants (13.1% vs. 17%). The area under the receiver operating characteristic curve for predicting SGA related complications was larger by the local reference (0.674, 95% CI: 0.67-0.677) than the INTERGROWTH-21st standard (0.658, 95% CI: 0.655-0.661) (P<0.001). The reclassification statistics showed negative improvement when applying the INTERGROWTH-21st standard instead of the local reference (net reclassification improvement: -0.037 (95% CI: -0.045 to -0.03), integrated discrimination improvement: -0.0031 (95% CI: -0.0039 to -0.0024)).
Conclusion. Compared to a local reference, the INTERGROWTH-21st birth weight standard fitted poorly for Chinese babies, especially those born <33 weeks' gestation.

关键字 birth weight; INTERGROWTH-21st standard; local reference; fitness

分类：16. Neonatology 新生儿
904

Adaptive challenges of family centered nursing in neonatal Pediatrics under the background of epidemic situation ——A qualitative study based on interviews between parents and medical staff

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Objective To understand the current status of family-centered care (FCC) in the neonatology department of the new coronavirus pneumonia (COVID-19) in the early stage of the COVID-19 pandemic, explore the impact of the new COVID-19 on the FCC, in order to provide science, effective guidance basis. Methods Using the phenomenological research method in the qualitative research, we conducted in-depth interviews with 20 doctors and nurses who worked in the NICU of a tertiary hospital in Shanghai from February 13 to 28, 2020, and 18 parents of neonates admitted to the department, Use Colaizzi analysis method to sort and analyze the data, and refine the theme. The results extracted the impact of the prevention and control measures under the COVID-19 epidemic on the FCC, which mainly included three themes: the negative emotions worried about being infected were prominent; parents' anxiety increased; medical staff generally responded actively. Conclusion In the early stage of the outbreak of COVID-19, NICU was severely restricted in implementing FCC. Doctors, nurses, and parents all experienced negative emotions such as anxiety and worry. Medical staffs need adequate training and education support to reduce possible future infectious diseases The impact of the outbreak on the FCC, ensuring the implementation and promotion of the FCC

关键字 COVID-19; NICU; family-centered care; psychological experience

分类：16. Neonatology 新生儿
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A Novel Algorithm with Paired Predictive Indexes to Stratify the Risk Levels of Neonates with Invasive Bacterial Infections: A Multicenter Cohort Study

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Background: Our aim was to develop a predictive model comprising clinical and laboratory parameters for early identification of full-term neonates with different risks of invasive bacterial infections (IBIs). Methods: We conducted a retrospective study including 1053 neonates presenting in nine tertiary hospitals in China from January 2010 to August 2019. An algorithm with paired predictive indexes (PPIs) for risk stratification of neonatal IBIs was developed. Predictive performance was validated using k-fold cross-validation. Results: Overall, 166 neonates were diagnosed with IBIs (15.8%). White blood cell count, C-reactive protein level, procalcitonin level, neutrophil percentage, age at admission, neurological signs, and ill-appearances showed independent associations with IBIs from stepwise regression analysis and combined into 23 PPIs. Using 10-fold cross-validation, a combination of seven PPIs with the highest predictive performance was picked out to construct an algorithm. Finally, 58.1% (612/1053) patients were classified as low-risk cases. The sensitivity and negative predictive value of the algorithm were 95.3% (95% confidence interval: 91.7-98.3%) and 98.7% (95% confidence interval: 97.8-99.6%), respectively. An online calculator based on this algorithm was developed for clinical use. Conclusions: The new algorithm constructed for this study was a valuable tool to screen neonates with suspected infection. It stratified risk levels of IBIs and had an excellent predictive performance.

关键字 neonates; invasive bacterial infections; risk stratification; paired predictive indexes; predictive model

分类：16. Neonatology 新生儿
916

Application of neonatal nutritional risk screening scale in hospitalized newborns in NICU

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Objective to understand the nutritional risk status and distribution characteristics of hospitalized newborns in NICU, and to clarify the direction for clinical nutritional support. Methods 500 newborns hospitalized in NICU in a pediatric hospital from January to March 2019 were selected by convenient sampling, and neonatal nutritional risk screening was used for nutritional risk screening. Results among the 500 hospitalized newborns, the incidence of high nutritional risk was 14.00% (70 cases), the incidence of moderate nutritional risk was 54.00% (270 cases), and the incidence of low nutritional risk was 32.00% (160 cases); The rank mean value of nutritional risk distribution of hospitalized newborns in term group (242.16) was lower than that in non term group (266.40), and there was significant difference ($P < 0.05$). Conclusion neonatal nutritional risk screening tool is feasible for newborns hospitalized in NICU, and attention should be paid to the nutritional risk screening of non term infants.

关键字 新生儿营养风险

分类：16. Neonatology 新生儿
928

Perioperative nursing care of 4 newborns with Pierre Robin sequence sign and difficult airway undergoing mandibular distraction osteogenesis

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The neonatal mortality of Pierre Robin sequence syndrome with difficult airway is as high as 30% ~ 65%. Solving airway obstruction and doing well airway management are the key. This paper summarizes the preoperative and postoperative nursing experience of 4 cases of Pierre Robin sequence sign with difficult airway for mandibular distraction osteogenesis. The key points of nursing included: trying to give airway opening and oxygen therapy support in prone or lateral position before operation, and endotracheal intubation under video laryngoscope or fiberoptic bronchoscope without improvement; Choose reasonable feeding methods to avoid choking; Keep the head in the middle and supine position after operation and strengthen airway management; Fixation and traction nursing of traction rod; Nursing care to prevent wound bleeding and infection; Pain care; Nutritional support; Family support.

关键字 Pierre Robin序列征；困难气道；下颌骨牵张成骨术；围术期护理

分类：16. Neonatology 新生儿
929

Fine management of severe infection and abscess secondary to puncture and suction of cap shaped subaponeurosis hematoma in a newborn

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Objective: To summarize the fine management of severe infection and abscess after puncture and suction of neonatal cap aponeurosis hematoma. Methods: firstly, the wound was evaluated in detail, including the general situation, nutrition and medication in the overall evaluation; Wound assessment and wound environment assessment (external force, wound infection, foreign body and pain) in local assessment. Neonatal stress injury risk assessment scale was used for external force and neonatal pain assessment scale (PIPP) was used for pain. Through detailed evaluation, we know the factors affecting wound healing. Then, the overall care of the wound shall be carried out. The appropriate cleaning solution shall be selected for each dressing change according to the wound infection. The sneaking part shall be cleaned and measured with a gastric tube to thoroughly clean the wound, and then debridement shall be given according to the specific situation of the wound. If necessary, mechanical debridement can be carried out in combination with surgery, because the wound infection is serious, The primary dressing is filled with silver dressing with significant antibacterial effect. At the same time, this dressing is also in line with the concept of wet healing. The appropriate dressing is selected according to the wound healing of children. After the infection symptoms are controlled, the lipid hydrocolloid dressing is used for filling, and the secondary dressing is gauze. Finally, use super elastic retention bandage with good air permeability and compliance to bind the head of children. Pay attention to the tightness during binding to avoid pressure injury. Add mesh elastic bandage outside the super elastic retention bandage to better fix the dressing. During the whole dressing change process, the neonatal pain was assessed as moderate pain. Oral ibuprofen was given to relieve pain and comfort pacifier was given according to the doctor's advice. After the use of the measures, it was assessed as mild pain and effectively reduce the pain. The risk of neonatal stress injury was assessed as low risk, but a water pillow was placed on the head to effectively prevent stress injury. Results: after detailed and complete evaluation, thorough cleaning and debridement of the wound, selection of appropriate dressing, and scientific management, the infection was controlled and the wound healing achieved satisfactory results. Conclusion: fine wound management can provide a wet healing environment, effectively promote wound healing, reduce pain, prevent stress injury and improve the quality of life of children.

关键字 cap shaped subaponeurosis hematoma; Infected; Abscess; Wound management;

分类：16. Neonatology 新生儿
1005

Clinical and genetic etiologies of neonatal unconjugated hyperbilirubinemia in the China Neonatal Genomes Project

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ABSTRACT
Background Neonatal unconjugated hyperbilirubinemia (NUCHB) is a common disorder in neonates. This study aims to investigate the clinical and genetic etiologies for neonates with NUCHB.
Study design Neonates with NUCHB were recruited retrospectively from the China Neonatal Genomes Project between August 2016 and September 2019. Clinical data and targeted panel sequencing data were collected and analyzed for all patients.
Results In total, 1412 patients with NUCHB were enrolled; 37% had total serum bilirubin levels that met recommendations for exchange transfusions. Known clinical etiologies were identified for 68% of the enrolled patients with the most common causes being multiple etiologies (16%), infection (15%), and breast feeding NUCHB (11%). For mild NUCHB and severe NUCHB, the most common causes were infection (17%) and multiple etiologies (21%), respectively. A genetic finding was made for 55 (4%) of the participants, including 45 patients identified with variants in genes associated with NUCHB and 10 patients with variants regarded as additional genetic findings. Among the 45 patients identified with NUCHB-related variants, the genes were mainly associated with enzyme deficiencies, metabolic/biochemical disorders, and red blood cell membrane defects. The top two genes in patients with NUCHB-related variants were G6PD and UGT1A1, which were detected in 34 (76%) of those patients.
Conclusions Known clinical etiologies, which varied with bilirubin levels, were identified in approximately two-thirds of the patients in our cohort. Infection and multiple etiologies were the most common clinical etiologies for mild NUCHB and severe NUCHB, respectively. Genetic findings were identified in 4% of the patients, with G6PD and UGT1A1 being the top two variant genes detected.

关键字 hyperbilirubinemia; etiology; targeted panel sequencing

分类：16. Neonatology 新生儿
1035

Characterization of Disease Phenotype in Very Preterm Infants with Bronchopulmonary Dysplasia : A Single Center Cross Sectional Study.

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Objectives: To investigate the frequency of four disease components: parenchymal lung disease, pulmonary hypertension (PH), large airway disease and rare gene mutation disease in preterm infants with BPD in Children’s Hospital of Fudan university. The association between each component and a primary composite outcome of death and hospitalization expenses was assessed.

Methods: Single center cross sectional study of infants born <32 weeks’ gestation with BPD who underwent chest Computed Tomography or sternum, echocardiography and neonatal PANEL test between 36-40 weeks postmenstrual age between 2017-2021. Moderate-severe parenchymal lung disease was defined by CTA or chest X-ray. PH was diagnosed by echocardiogram. Large airway disease was defined as tracheomalacia or bronchomalacia on bronchoscopy. Rare gene mutation disease was diagnosed by PANEL test.

Results: Of 16443 evaluated infants, 511 were classifiable into phenotypic subgroups: 450 with moderate-severe parenchymal disease, 120 with PH, 50 with large airway disease and 10 with gene mutation. Individually, PH and large airway disease, but not moderate-severe parenchymal disease, were associated with increased risk for the primary study outcome of death. Having more disease components was associated with an incremental increase of hospitalization expenses.

Conclusions: Infants with BPD are variable in pathophysiology. Disease phenotyping may enable better risk stratification and more rational medical treatments.

关键字 支气管肺发育不良、早产儿、疾病表型

分类：16. Neonatology 新生儿
1075

Clinical features and prognostic factors prediction of poor neurodevelopmental outcomes in infantile hydrocephalus

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Background: Summarize the clinical characteristics of infantile hydrocephalus and analyze the prognostic factors of poor neurodevelopmental prognosis.

Method: The demographic data, clinical characteristics, and EEG of children diagnosed with hydrocephalus in the Neonatal Ward of Peking University First Hospital from 2008.1.1 to 2019.12.31 were collected retrospectively. Head ultrasound indices include: ventricular index (VI), ventricular height (VH) and thalamo-occipital distance (TOD). Follow-up to corrected age 20-24 months after discharge, the neurodevelopmental prognosis of the infants is divided into a good prognosis group: the Bayley-I development scale or Griffiths mental development scale indicate that the children have an average development quotient Score ≥70 points without the visual and hearing impairment, epilepsy and cerebral palsy. The poor prognosis group has any of the following: 1) development quotient average score of scales <70; 2) epilepsy; 3) hearing impairment; 4) visual impairment; 5) cerebral palsy; 6) die. To compare the prognosis of hydrocephalus caused by different causes, and predict the factors of poor neurodevelopmental prognosis.

Results:
1. Demographics: A total of 137 children were enrolled, with an average gestational age of 35.5±4.1 weeks, a birth weight of 2501.9±973.2g, and the sex ratio M/F is 1.91. 41 cases had convulsions (30%), and finally 6 cases were diagnosed as epilepsy.
2. Etiology: 129 cases of acquired hydrocephalus, the causes include periventricular-intraventricular hemorrhage (45%), meningitis (23%), both hemorrhage and meningitis (15%), inherited metabolic diseases (8%, of which 82% was Methylmalonic aciduria), tumor/cyst/mass lesions (3%). 8 cases were congenital hydrocephalus or the etiology is unknown.
3. Analysis of prognostic factors:
①Different causes of poor prognosis accounted for: intraventricular hemorrhage 40.7%, meningitis 46.4%, both hemorrhage and meningitis 52.9%, inherited metabolic diseases 90.9%.
②There was no statistical difference between the two groups of children in gender, gestational age, age at presentation, convulsion, type of intervention, protein and glucose content of cerebrospinal fluid, and aEEG (when the disease was most severe) (P>0.05).
③The earliest treatment time of the poor prognosis group was 31.1±8.4 days after the diagnosis of hydrocephalus, which was significantly longer than the good prognosis group 10.3±41.3 days; the level of cranial ultrasound VI, VH, TOD (VI: left 2.47 cm, right 2.46 cm; VH: left 2.34cm, right 2.20cm; TOD: left 3.33cm, right 3.16cm), significantly greater than the good prognosis group (VI: left 2.10cm, right 1.98cm; VH: left 1.73cm, right 1.65cm; TOD: left 2.79cm, Right 2.44cm). The initial treatment time of hydrocephalus>13.5 days, the sensitivity of predicting poor prognosis is 66.7%, and the specificity is 75.5%. The VI value of cranial ultrasound> 2.12 cm, the sensitivity of predicting poor prognosis is 64.3%, and the specificity is 68.4%; the VH > 1.82 cm, the sensitivity of predicting poor prognosis is 67.3%,

and the specificity is 70%; the TOD > 2.60 cm, the sensitivity for predicting poor prognosis was 56.3%, and the specificity was 85.0%.

Conclusions: The common causes of infant hydrocephalus are intraventricular hemorrhage and meningitis (83%). Attention should be paid to inherited metabolic diseases (methylmalonic aciduria, etc.); the prognosis of hydrocephalus caused by intraventricular hemorrhage is relatively good (40.7%), compared with inherited metabolic disease (90.9%). It is found that the late treatment times of hydrocephalus (>13.5 days) and severe ventricular dilatation (VI>2.12cm, VH>1.82cm, TOD>2.60cm) indicate a poor prognosis.

关键字 neurodevelopmental outcomes, infantile hydrocephalus, prognosis, prediction

分类：16. Neonatology 新生儿

1102

Association between Hemodynamically Significant Patent Ductus Arteriosus and Severe Neonatal Morbidity

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Objective: To assess whether the duration and magnitude of the shunt with patent ductus arteriosus (PDA) are related to a higher incidence of severe intraventricular hemorrhage, bronchopulmonary dysplasia (BPD) or death.
Study design: A total of 135 infants with gestational age less than 28 weeks were evaluated retrospectively between 2010 and 2020; 15 (11.1%) developed severe intraventricular hemorrhage (IVH group) and 46(34.1%) developed BPD or died (BPD group) .Prenatal and neonatal risk factors for severe neonatal morbidity were analyzed using univariate and multivariate analyses. A review of all echocardiographic evaluations performed from birth up to 36 weeks of postconceptional age or final ductal closure was carried out, to detect the presence of PDA, and estimate the severity of ductal shunt with ductal diameter (DD) . PDA was classified as hemodynamically nonsignificant (E1)(DD≤ 1.5 mm), moderate (E2) (1.5mm < DD ≤ 2.5 mm) and severe hemodynamically significant (E3)(DD > 2.5 mm).
Results: The duration of E3 PDA (11.5 versus 0.0 days; p<.001) and hs-PDA (E2 and E3) (30.5 versus 11.5 days; p<.001) were greater in BPD group versus non-BPD group. The duration of E3 PDA (14.5 versus 3.0 days; p<.001) was greater in IVH group versus non-IVH group. Lower gestational age, birth weight, prolonged duration of mechanical ventilation, higher rate of inotrope use and PDA ligation were associated with development of severe neonatal morbidity. After adjusting for confounders, the rate of inotrope use (OR: 2.659 [95%CI: 1.000, 7.069]; p =0.050), the duration of E3 PDA (OR: 1.058 [95%CI: 1.014, 1.103]; p =0.009), and mechanical ventilation (OR: 1.118 [95%CI: 1.061, 1.179]; p <0.001), were independently associated with development of BPD or death. Persistence of E3 PDA (OR: 1.042 [95%CI: 1.001, 1.085]; p =0.044), and prolonged duration of mechanical ventilation for more than 7 days (OR: 6.602 [95%CI: 1.898, 22.958]; p =0.003), were independently associated with development of severe intraventricular hemorrhage.
Conclusions: Persistence of severe hemodynamically significant PDA is associated with severe neonatal morbidity. The optimal management of hs-PDA is helpful to improve neonatal outcomes.

关键字 patent ductus arteriosus，hemodynamically significant PDA，bronchopulmonary dysplasia，severe intraventricular hemorrhage

分类：16. Neonatology 新生儿

1161

Impacts of Enriched Human Milk Cells on Fecal Metabolome and Gut Microbiome of Premature Infants with Stage I Necrotizing Enterocolitis: A Pilot Study

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Scope: Necrotizing enterocolitis (NEC) is a leading cause of morbidity and mortality in preterm infants, occurring more often in formula-fed infants than in breastfed infants. Recent animal studies have shown that cells in fresh breast milk survive in the newborns' digestive tract. However, no clinical studies have been conducted on the effects of human milk cells, and their biological roles in the infants' intestines remain unexplored.

Methods and Results Cells from fresh milk of their own mothers were enriched and fed to premature infants with Bell's Stage I NEC once a day for seven days since the onset of NEC. Fecal samples were collected at enrollment and two weeks later, and the calprotectin levels, metabolome, and microbiome of these samples were analyzed. Fecal sphingolipids were observed to be enriched in NEC patients and positively correlated with calprotectin levels. Following intervention with enriched human milk cells, inflammation-associated sphingolipids and microbiome profiles were altered and resembled those of the controls.

Conclusion These preliminary findings provide insight into the roles of fecal sphingolipid metabolism in the neonates' intestinal inflammation and reveal the potential impacts of enriched human milk cells on premature infants with Bell's Stage I NEC, indicating the need for further investigation.

关键字 necrotizing enterocolitis, intestinal metabolome, fecal calprotectin, gut microbiome, human milk cell

分类：16. Neonatology 新生儿

1171

Use of medical exome sequencing for identification of underlying genetic defects in NICU: experience in a cohort of 2,303 neonates in China

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Background: Emerging evidence demonstrates the clinical utility of genomic applications in newborn intensive care unit (NICU) patients with strong indications of Mendelian etiology. However, such applications' diagnostic yield and utility remain unclear for NICU cohorts with minimal phenotype selection.
Methods: In this study, focused medical exome sequencing was used as a first-tier, singleton-focused diagnostic tool for 2,303 unrelated sick neonates. Integrated analysis of single nucleotide variants (SNVs), small insertions and deletions (Indels), and large copy number variants (CNVs) was performed.
Results: The diagnostic rate in this NICU cohort is 12.3% (284/2303), with 190 probands with molecular diagnoses made from SNV/Indel analyses (66.9%), 93 patients with diagnostic aneuploidy/ CNVs findings (32.8%), and 1 patient with both SNV and CNV (0.4%). In addition, 54 (2.3%) of patients had a reportable incidental finding. Multiple organ involvements, craniofacial abnormalities, and dermatologic abnormalities were the strongest positive predictors for a molecular diagnosis. Among the 190 cases with SNV/Indel defects, direct impacts on medical management were observed in 46.8% of patients after the results were reported.
Conclusion: In this study, we demonstrate that focused medical exome sequencing is a powerful first-line diagnostic tool for NICU patients. Significant number of diagnosed NICU patients can benefit from more focused medical management and long-term care.

关键字 NICU, medical exome, diagnostic rate, incidental findings, clinical managemen

分类：16. Neonatology 新生儿

1187

Epidemiology of necrotizing enterocolitis in preterm infants in China: a multicenter cohort study from 2015 to 2018

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ObjectiveTo describe the currentincidence, case-fatality rate and surgical treatment proportion of necrotizing enterocolitis (NEC) among preterm infants in China.

MethodsBetween May 2015 and April 2018, live neonates born <34 weeks of gestational age (GA) and admitted to participating NICUs within 7 days of birth were included, from twenty-five tertiary hospitals of 19 provinces. Infants who had major congenital malformations or died within 3 days of birth were excluded. Data were prospectively collected by trained abstractors, using the originally created database for a randomized clustered controlled study entitled “Reduction of Infection in Neonatal Intensive Care Units using the Evidence-based Practice for Improving Quality” (REIN-EPIQ study, clinicaltrials.gov #NCT02600195). NEC was defined as ≥stage IIaccording to Bell’s criteria.

ResultsA total of 24731 infants were included, of which 23101 infants received complete care. Among infants received complete care, the overall incidence of NEC was 3.3% (768/23101) and decreased with increasing GA and birth weight. The incidence of NEC was 4.8% (568/11744) in very preterm infants (VPIs) and1.8% (200/11357) in infants born ≥32 weeks GA, respectively. The overall case-fatality rate of NEC was 9.5% (73/768), and also decreased with increasing gestational age and birth weight. A total of 214 (27.9%) patients underwent surgery, and their overall case-fatality rate was 13.6% (29/214). There were 73 (34.1%) patients underwent laparotomy alone, 13 (6.1%) patients received peritoneal drainage alone, and 128 (59.8%) patients underwent both laparotomy and peritoneal drainage. Among surgically treated patients, the case-fatality rate was 13.2% (24/182) in VPIs and 15.6% (5/32) in infants born ≥32 weeks GA, respectively. Significant variation of incidences of NEC existed among different centers (0.6%-11.1%). The variation remained significant after adjustment.

ConclusionsThe incidence and case-fatality rate of NEC are high in China, especially among infants with GA ≥32 weeks, and varies significantly among sites. A high proportion of NEC infants required surgical management, with an even higher case-fatality rate. Further quality improvement measures are needed to reduce site variations and ensure more infants receive complete care.

关键字 necrotizing enterocolitis, preterm infant, China

分类：16. Neonatology 新生儿

1202

Thrombocytopenia in infants with perinatal asphyxia

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Background: To discuss the risk factors of neonatal thrombocytopenia after perinatal asphyxia.
Method: This was a retrospective study that included neonates with perinatal asphyxia in our hospital from June 2019 to December 2020. Maternal and neonatal information of all infants were recorded. T-test, Fisher’s exact test, chi-square test and Logistic regression were performed to explore the risk factors of neonatal thrombocytopenia and to compare the perinatal outcomes of newborns with or without thrombocytopenia.
Results: A total of 122 newborns with perinatal asphyxia were included. Among them, 16 cases had thrombocytopenia and 106 cases did not suffer from thrombocytopenia. The incidence of thrombocytopenia was 13.11%. Within 2 weeks after birth, the lowest point of the platelet count was the 8th day, and the platelet count was 225.38±124.88×10^9/L. Factors related to thrombocytopenia include small gestational age, low birth weight, and low 1-minute Apgar score. Logistic regression analysis showed that thrombocytopenia was associated with low gestational age (OR 0.702, 95% CI 0.576, 0.855, P = 0.000) and low 1-minute Apgar score (OR 0.683, 95% CI 0.494, 0.944, P=0.021). The proportion of neonates with thrombocytopenia requiring invasive respiratory support was higher than that of neonates without thrombocytopenia (37.5% vs 9.43%, P=0.007).
Conclusions: Neonatal thrombocytopenia is likely to occur in perinatal asphyxia infants with small gestational weeks and low 1-minute Apgar scores. Infants with thrombocytopenia are more likely to require invasive respiratory support.

关键字 thrombocytopenia, perinatal asphyxia, risk factor

分类：16. Neonatology 新生儿

1211

Caffeine Therapy for Apnea of Prematurity: Role of the Circadian CLOCK Gene Polymorphism

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Background: Frequent apnea may be one of the most troublesome problems in the neonatal intensive care unit. Standard-dose caffeine citrate has been routinely prescribed for apnea of prematurity (AOP) management based on its clear benefits and safety; however, some preterm infants respond well to the therapy, but others do not. The AOP phenotype has been attributed solely to immature control of respiratory system consequent to preterm birth but there also be important genetic influences. Therefore, how genetics may influence the efficacy of caffeine in preterm infants should be better explored. Based on our previous report, herein, we tested the hypothesis that the polymorphisms of the human Circadian Locomotor Output Cycles Kaput (*CLOCK*) gene, encoding one of the two core components of the circadian rhythm, would be involved in the response to caffeine citrate therapy in preterm infants. This study also touched on circadian clock interactions with aryl hydrocarbon receptor (AHR) signaling pathways in these preterm babies who received caffeine citrate.

Method: This single-center study collected data from 112 preterm infants (< 35 weeks' gestational age) between July 2017 and July 2018 including apnea-free (n = 48) and apneic (n = 64) groups. Eighty-eight candidate single-nucleotide polymorphisms (SNPs) in 9 human genes, including *CYP1A2*, *CYP3A4*, *CYP3A5*, *CYP3A7*, *AHR*, *AHR* repressor (*AHRR*), aryl hydrocarbon receptor nuclear translocator (*ARNT*), Brain and Muscle ARNT-Like 1 (*BMAL1* ; also known as aryl hydrocarbon receptor nuclear translocator-like protein 1, *ARNTL1*), and *CLOCK*, were tested by a MassARRAY system. The allele and genotype frequencies of various genes were examined for deviation from the Hardy–Weinberg equilibrium (HWE) using the goodness-of-fit chi-square test. Distributions of genotype among neonates in the apneic and apnea-free groups were compared using the goodness-of-fit chi-square test. The Benjamini–Hochberg false discovery rate (FDR) was used for multiple hypothesis testing, and the adjusted *P* value (P_{FDR}) was obtained. Multivariable logistic regression analysis was established through variable screening to explore the effect of significant outcomes from the univariate analysis of apneic and apnea-free groups. *P* values < 0.05 were considered to be statistically significant. The association analysis was estimated by using the PLINK Whole genome data analysis Toolset and SNPStats software. Linkage disequilibrium (LD) and haplotype analysis were evaluated using the Hapview software.

Results: No significant intergroup differences in allele distributions or genotype frequencies of the genes, i.e., *CYP1A2*, *CYP3A4*, *CYP3A5*, *CYP3A7*, encoding CYP450 proteins correspondingly, were found in our study preterm babies. Two more SNPs in AHR gene, but not in *AHRR* or *ARNT* genes, were found to be associated with the response to caffeine citrate therapy in our pediatric patients. Notably, in the 46 candidate SNPs in *CLOCK* gene, 26 SNPs were found to be associated with the response to caffeine treatment in these babies. Interestingly, the significant association still retained for 18 SNPs in *CLOCK* gene after false discovery rate correction. Moreover, strong LD formed respectively in those variants in *AHR*, *ADORA2A*, and *CLOCK* genes was confirmed to be associated significantly with better response to standard-dose caffeine therapy.

Conclusions: In summary, the genetic polymorphisms of *CLOCK* gene polymorphisms are involved in the response to caffeine therapy for neonates with AOP, which indicated that circadian rhythm may play essential roles in the response to caffeine therapy. Whether the AHR- and CLOCK- signaling pathways interact with each other in the caffeine treatment remains largely unclear. Future clinical studies by recruiting more immature babies and basic research are needed to explore how circadian rhythm affects the response to caffeine therapy.

关键字 Preterm infant; Apnea of prematurity; Caffeine; circadian rhythm; CLOCK, AHR; Polymorphism

分类：16. Neonatology 新生儿
1214

Changes in pathogens of neonatal bacterial meningitis over the past 10 years: a single-center retrospective study

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Background: Bacterial meningitis is a serious central nervous system infection associated with high morbidity and mortality during the neonatal period, while the pathogen distribution was rarely reported on a large scale in China. This study aimed to investigate the distribution and change trends of neonatal bacterial meningitis pathogens in Children’s Hospital of Fudan University over the past 10 years.
Methods: We performed a retrospective study of all cases diagnosed with neonatal bacterial meningitis and admitted to our hospital from April 2008 to March 2018. The differences of pathogen distribution between preterm and full-term infants, early-onset and late-onset infection, the first five-year and the second five-year epoch were investigated.
Results: 195 cases were enrolled, including 110 (56.4%) for male, 60 (30.8%) for premature infants, 41 (21%) for early-onset meningitis. The most common pathogens were Escherichia coli (E. coli) (37.9%) and Group B Streptococcus (GBS) (17.4%). Gram-negative bacteria were more common in preterm infants than in full-term infants (P=0.001). GBS was only detected in full-term infants (P=0.000); Klebsiella pneumoniae (P=0.000) and Enterobacter cloacae (P=0.007) were more common in preterm infants. Gram-positive bacteria were more frequent in early-onset meningitis than in late-onset meningitis (P=0.013). Both E. coli (44.5% vs. 29.4%, P=0.031) and GBS (22.7% vs. 10.6%, P=0.027) infections increased significantly in the epoch from April 2013 to March 2018 compared with the epoch from April 2008 to March 2013.
Conclusions: GBS and E. coli are the most common pathogens of neonatal bacterial meningitis in our hospital, and both have shown an upward trend over the past 10 years.

关键字 neonates; bacteria; meningitis; pathogen; trend

分类：16. Neonatology 新生儿
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Ggenetic analysis of a neonatal with Finnish congenital nephrotic syndrome: A case report

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ABSTRACT
Objective: To explore the clinical characteristics and the mutation type of congenital nephrotic syndrome, in order to provide reference for this kind of disease.
Methods: Clinical characteristics and NPHS1 gene test report of a neonatal with congenital nephrotic syndrome Finnish type and his parents were retrospectively analyzed.
Results: A boy was born prematurely at 36+4 weeks of gestational age, 8 hours after birth showed clinical manifestations of nephrotic syndrome: proteinuria, hypoproteinemia and severe edema, the clinical diagnosis was congenital nephrotic syndrome, confirmed by gene sequencing as finnish type, her mother checked out pathogenic mutations Chr19: : 35831358 G > A, father Chr19: detection of pathogenic mutations: 35842406 G > A.
Conclusion: The baby inherited the recessive gene mutated by their parents, which is a compound heterozygote. This conclusion provides an important reference for the genetic counseling and prenatal diagnosis of this family.

关键字 congenital nephrotic syndrome; finnish type; NPHS1; gene mutation

分类：16. Neonatology 新生儿
1220

Nursing management of neonatal Chitrin protein deficiency: A case report

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【Abstract】
Objective: To investigate the clinical characteristics and gene mutation types of a neonatal case of Sitrin deficiency in order to provide a reference for clinical treatment of this kind of disease.
Methods: The clinical data and treatment of one child with Chitrin deficiency were retrospectively analyzed.
Results: Male infant A, 38+2 weeks of gestational age, was referred to our hospital because of extreme high blood bilirubin, after admission to neonatal extreme high bilirubin levels, active treatment effect is not obvious, poor gradually appear, convulsions, recurring coagulant function abnormality and low serum albumin leels, elevated bilirubin repeatedly, such as liver a gradual increase in performance. After clinical symptomatic support treatment, the symptoms were still not alleviated obviously. Therefore, considering the possibility of genetic metabolic disease in this case, relevant examinations were immediately improved, and total blood bile acid determination, blood high pressure liquid chromatography-tandem mass spectrometry and urine gas mass spectrometry organic acid detection indicated that the child was chitrin protein deficiency. Breast-feeding and antibiotic treatment were stopped immediately, and lactose free deep hydrolyzed protein formula was given. Meanwhile, fat-soluble vitamins were supplemented, and fresh frozen plasma was injected to improve coagulation. After careful nursing, her symptoms improved significantly, and she was discharged on January 28.
Conclusion: For autosomal recessive hereditary disease, the disease incidence is low, more than normal at birth, characterized by cholestasis after sex icteric, accompanied by hepatomegaly, liver function damage, coagulant function abnormality, subcutaneous bleeding and other clinical manifestations, the general treatment is invalid or deteriorating condition, unclear or clinical diagnosis with other disease cannot explain, should be highly suspected genetic metabolic diseases. There is no specific and effective treatment for this disease. Once the diagnosis is made, the patients should be fed with milk powder without lactose hydrolyzed protein, and liver function and blood amino acid concentration should be monitored regularly.

关键字 Chitrin protein deficiency; Pathogenic gene; The newborn; Case report; nursing

分类：16. Neonatology 新生儿
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Neonatal necrotizing enterocolitis caused by umbilical arterial catheter-associated abdominal aortic embolism: A case report

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【Abstract】
Objective: To investigate the cause and treatment of necrotizing enterocolitis caused (NEC) by umbilical arterial catheter (UAC)-associated abdominal aortic embolism in neonates, in order to provide reference for clinical such diseases.
Methods: The clinical data and treatment of one patient with necrotizing enterocolitis caused by abdominal aortic embolism after umbilical arterial catheter extubation were retrospectively analyzed.
Results: Female infant A, 21 min of age, weighing 830 g at 28+6 weeks of gestational age, was referred to our hospital because of premature birth and shallow breathing. The umbilical arteriovenous catheter was inserted on the day after birth, and the catheter was pulled out 9 days later. Within 48 hours after extubation, the patient's manifestations included poor responsiveness, heart rate range of 175-185/min, and currant jelly stool. Therefore, we considered a diagnosis of NEC. Partial abdominal aortic embolism (2cm×0.3cm), abdominal effusion and neonatal necrotizing enterocolitis were confirmed by B-mode ultrasound. The patient was treated with nil per os(NPO), gastrointestinal decompression, anti-infective therapy, blood transfusion, and low-molecular-weight heparin sodium Q12H for anticoagulant therapy (from May 20 to June 1, the dosage of low-molecular-weight heparin sodium was adjusted according to the anti-Xa activity during treatment). On the 67th day after admission, the patient fully recovered and was discharged.
Conclusion: The abdominal aortic thrombosis in this patient was considered to be catheter related, which requires immediate treatment once diagnosed. The choice of treatment should be determined according to the location of the thrombus and the patient's condition.

关键字 Umbilical arterial catheter; abdominal aortic thrombosis; necrotizing enterocolitis; neonate; case report

分类：16. Neonatology 新生儿
1226

Effect of four different positions on gastric emptying in preterm infants: A network Meta-analysis

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[Abstract] Objective to evaluate the effect of different body positions on gastric emptying in preterm infants, and to provide evidence for postural management after feeding. Methods Search Cochrane Library, Web of Science, Pubmed, MEDLINE (Ovid), Central (Ovid), Embase (Ovid) , SinoMed, Wanfang Database, CNKI and manual search. A Randomized controlled trial study and Cohort studies were conducted to compare the effects of different body positions on gastric emptying in preterm infants. After literature screening, literature quality evaluation and data extraction, we used Review manager and ADDIS to do direct comparison Meta-analysis and net-work Meta-analysis, at the same time, Draw Mesh relationship map. Results A total of 1764 subjects were enrolled in this study, including 9 English and 6 Chinese literatures. The consistency model showed that supine position VS prone position [SMD = 5.62, 95% CI: (0.46, 10.86)] , prone position VS left lateral position [SMD =-9.43,95% CI: (-15.87, -3.12)] , supine position VS right lateral position [SMD = 7.02, 95% CI: (0.74, 13.48) , left VS right lateral position [SMD = 10.90, 95% CI: (4.24, 17.41)] had significant difference in the effect of gastric emptying in preterm infants (P<0.05) , supine VS left decubitus position [SMD =-3.86, 95% CI: (-10.44, 2.88)] , right lateral position VS prone position [SMD =-1.41, 95% CI:(-7.46, 4.50)] had no significant difference (P>0.05) . The results of area ranking under cumulative ranking probability curve showed that right lateral decubitus position had the best effect on gastric emptying, followed by prone position. The results of node analysis showed that the direct comparison was consistent with the indirect comparison (P>0.05). Conclusion right lateral position and prone position are effective in improving gastric emptying in preterm infants, but more high quality, multi-center and large sample Randomized controlled trial are needed.

关键字 Body position; Preterm infant; Gastric residuals; Network meta-analysis; evidence-based care

分类：16. Neonatology 新生儿
1227

Best evidence summary of artificial management in neonates

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[Abstract] Objective: to search, evaluate, and summarize the best evidence of artificial airway management in neonates at home and abroad. Method: search for BMJ best practice, UpToDate, BMJ Clinical evidence, National Guidelines Clearinghouse (NGC), Scottish Intercollegiate Guidelines Network (SIGN), Guidelines International Network (GIN), National Institute for Health and Clinical Excellence (NICE), Chinese Clinical Guidelines library. At the same time, we searched the relevant evidence about artificial airway management in the databases of Joanna Briggs Institute Library (JBI), Medline, Embase, Cochrane Library, PubMed, Sinomed, CNKI, Wanfang, including clinical decision-making, guidelines, summary of evidence, systematic review and expert consensus. The retrieval period was from the inception of databases to October 2020.The included literatures were independently evaluated by two researchers and evidence was extracted from the literature that met the quality criteria. Results: A total of 16 articles were collected to form 32 best evidence from 7 aspects: postural management, nebulization, intratracheal aspiration, airway lavage, airway humidification, analgesia and sedation, and prevention of complications. Conclusions: This study summarizes the best evidence of artificial airway management in newborns and provides evidence-based basis for clinical staff to formulate reasonable artificial airway management programs for newborns, standardize artificial airway management, and ensure the safety of neonates.

关键字 Infant, Newborn; Respiration, Artificial; Airway Management; Evidence-Based Nursing

分类：16. Neonatology 新生儿
1228

Risk management of central venous catheterization nursing in extremely low birth weight infants

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[Abstract] Objective: To explore the risks in the intravenous tube process of ultra-low birth weight children's centers and provide reference for clinical practice. Method:The risk management measures such as temperature management, skin protection, pain management, neuroprotection strategy and prevention of de-tube were reviewed by means of the timing of the venous tube in the ultra-low birth weight child's center and the temperature management, skin protection, pain management, neuroprotection strategy and prevention of de-tube removal. Results: (1) For ultra-low birth weight children should be placed in UVC immediately after birth, retained for 7 to 14 days, to improve circulation, edema reduction, peripheral blood vessels after the removal of UVC continued to PICC placed, can reduce the external peripheral veins Damage; (2) Clinically, according to the hospital NICU ambient temperature and material conditions combined with the condition of the child to choose radiation table, plastic film, heating iodine volt, heating gel mattress and other comprehensive heating measures, at the same time, the need to dynamically monitor the temperature of the child, so as to avoid high fever ;(3) in the tube and maintenance process should take a series of measures to avoid chemical skin burns and medical adhesive-related skin damage; (4) in the line PICC tube 60 minutes before the choice of EMLA cream for local application, tube control process supplemented by touch, non-nutritional sucking and other means of distraction, to achieve the goal of pain prevention; That is, within 72 hours of birth to avoid punctured PICC to reduce the risk of intracranial bleeding, if you must choose PICC tube, should be preferred by lower limb tube, combined with cavity inner electricity (EKG) and B super positioning. Conclusions: Central intravenous tube plays an active role in the treatment of ultra-premature and ultra-low birth weight, but there are many risks in the process of tube control, only early to evaluate the reasonable choice of timing, in the process of control strictly do a good job of temperature management, skin protection management, pain management, neuroprotective strategy early prevention of intracranial bleeding and anti-de-tube risk management to minimize the risk, thereby improving the survival rate and survival quality of extremely preterm infant and extremely low birth weight children.

关键字 Extremely low birth weight infant; Central venous catheters; Risk management

分类：16. Neonatology 新生儿
1230

Bovine lactoferrin in preventing sepsis and necrotizing enterocolitis in preterm infants: a Meta-Analysis

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Objective To systematically analyze the effect of bovine lactoferrin on the prevention of sepsis and necrotizing enterocolitis in preterm infants. **Methods** The computer searched the randomized controlled trials of bovine lactoferrin in the prevention of sepsis and necrotizing enterocolitis in preterm infants . According to the inclusion and exclusion criteria, the literature was screened, the data was extracted and the literature quality was evaluated, and the Revman 5.4 software was used for Meta-Analysis. **Results** 8 randomized controlled trials involving 5091 preterm infants were included. Meta-Analysis results show that bovine lactoferrin can effectively prevent the occurrence of late-onset sepsis in preterm infants [OR=0.84, 95%CI (0.72, 0.97), P=0.02], but it can not prevent necrotizing enterocolitis and other diseases in preterm infants (P>0.05). **Conclusion** Bovine lactoferrin, as an enteral supplement, can effectively prevent late-onset sepsis in preterm infants. However, large samples and high-quality RCTs are still needed for verification.

关键字 lactoferrin; preterm; infant; sepsis; necrotizing enterocolitis; Meta-Analysis

分类：16. Neonatology 新生儿
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Design and application of five-ring two-way training system for newly recruited nurses based on ISD model

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[Abstract] Objective Based on the Instructional System Design (ISD), a five-ring two-way training system for newly recruited nurses is designed to provide a theoretical basis for the training of newly recruited nurses in our hospital. Methods A historical control design was adopted, and newly recruited nurses in the Department of Neonatology of West China Second Hospital of Sichuan University were selected as the research subjects. The subjects were included as the control group (n=58) from September 1, 2019 to July 1, 2020, and the routine mode was adopted. Training: The trial group (n=46) will be included from September 1, 2020 to July 1, 2021, and the five-ring two-way training system will be used for training. Take the number of document writing errors from January 1st to July 1st in the two groups, daily (10 months)/end-of-semester theoretical results, daily (10 months)/end-of-semester operating results, and the results of the nurse core competency scale as The evaluation index evaluates its application effect. The Chi-square test was used to compare the basic data of the two groups, and the T test was used to compare the results of the two groups.Methods A historical control design was adopted, and newly recruited nurses in the Department of Neonatology of West China Second Hospital of Sichuan University were selected as the research subjects. The subjects were included as the control group (n=58) from September 1, 2019 to July 1, 2020, and the routine mode was adopted. Training: The trial group (n=46) will be included from September 1, 2020 to July 1, 2021, and the five-ring two-way training system will be used for training. Take the number of document writing errors from January 1st to July 1st in the two groups, daily (10 months)/end-of-semester theoretical results, daily (10 months)/end-of-semester operating results, and the results of the nurse core competency scale as The evaluation index evaluates its application effect. The Chi-square test was used to compare the basic data of the two groups, and the T test was used to compare the results of the two groups.Results After the implementation of the five-ring two-way training system for newly recruited nurses based on the ISD model, the number of newly recruited nurses in the experimental group was reduced (5.54±3.845 points), daily theory (97.257±0.911 points), and daily operation exams (97.256± 1.164 points) were improved, the difference was statistically significant (P<0.05), the final theory (71.609±5.530 points) and the final operation (93.902±1.751 points) were not statistically significant (P≥0.05), consider the question bank design Questions are related to changes; in the comparison of the results of the Core Competence Scale, it is found that the evaluation intervention ability (3.494±0.412 points), leadership ability (3.623±0.489 points), management ability (3.755±0.283 points), and communication ability (3.970±0.496 points)), teaching ability improved (3.149±0.834 points), the difference was statistically significant (P<0.05).Conclusion The five-ring two-way training system for newly recruited nurses based on the ISD model can improve the clinical nursing ability and core competence of newly recruited nurses, and is worthy of clinical application.

关键字 ISD model; New induction training; training system

分类：16. Neonatology 新生儿
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The practice of Quality Control Circle to improve the Colostrum Feeding rate of Premature Infants under Mother-Infant Separation

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[Abstract]
Objective To explore the application effect of quality control circle in improving the colostrum feeding rate of premature infants under mother-infant separation.
Methods A quality control circle was established in March 2019. The standard process of the quality control circle was used to find and analyze the colostrum feeding situation and influencing factors of premature infants under mother-infant separation, and intervene in the theme selection, activity type determination, plan formulation, and status quo. , Target value setting, true cause analysis, make full use of tools such as 5W1H on-site checklist and Plato to investigate and analyze maternal colostrum feeding willingness and neonatology nurses' colostrum feeding compliance, and formulate countermeasures based on relevant results and implement them , Use gold data software for data collection, enter the data into SPSS 25.0 for analysis, and use 2 test for counting data. P<0.05 indicates statistical significance. Finally, the content of this event will be reviewed, and the results will be standardized and further promoted.
Results After taking corresponding measures to intervene, data collection was carried out. After verification, the colostrum feeding rate under mother-infant separation increased from 63.59% to 88.39%, and the target achievement rate was 109.83%. Knowing whether the child has breast milk and not understanding the importance of colostrum is effective in improving the items, the difference is statistically significant (P<0.05), and the fruitless effect is significant.
Conclusion The implementation of quality control circle activities has a significant effect on improving the colostrum feeding rate of premature infants under mother-infant separation, and the comprehensive capabilities of the circle members have been improved. The standardization results under multidisciplinary cooperation are significant, which can provide implementation experience for other breast milk bank operation guarantee units. Provide assistance for the successful implementation of colostrum feeding in premature infants.

关键字 human colostrum; preterm infant; mother-infant separation; quality control circle

分类：16. Neonatology 新生儿
1234

PICC catheterization and management of 8 newborns with permanent left superior vena cava

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[Abstract] Objective To discuss the Peripherally Inserted Central Catheter(PICC)catheteri-zation method of neonates with permanent left superior vena cava(PLSVC) 。Methods A retrospective analysis of the clinical data of 8 PLSVC neonates admitted to our hospital from January 2017 to June 2020, as well as the PICC catheterization process and management experience。Results In 8 PLSVC, One case was type II PLSVC. After successful puncture, ultrasound showed a right-to-left shunt, and the lumen of the left superior vena cava was significantly smaller than that of the right superior vena cava. Therefore, it was removed on the same day and the lower limbs were to be re-inserted. The family members signed it 12 hours after admission The treatment was given up and the child was taken away; the other 7 patients were planned to be extubated after the PICC catheter was indwelled for 6 to 39 days. During the indwelling period, no PICC-related complications occurred, and no serious complications such as arrhythmia and pericardial tamponade occurred. Conclusion The key points of nursing care for PLSVC neonatal PICC include: reasonable selection of the timing of catheterization, retrospective analysis of the child’s imaging data before catheterization, correct measurement of the body surface length, and placement of the PICC catheter tip in the left superior vena cava under ultrasound guidance. The middle and lower 1/3 places; close observation during catheter use, early identification of PICC-related complications and corresponding treatment; establishment of special case files to ensure the safe use of PICC in neonates with permanent left superior vena cava.

关键字 PLSVC; PICC; infant, neonate

分类：16. Neonatology 新生儿
1235

Secondary necrotizing enterocolitis after the failure of patent ductus arteriosus closure of an extremely low birth weight at 25+4 week of gestational age

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[Abstract] Objective: To explore the causes, treatment and treatment of secondary necrotizing enterocolitis after the failure of arterial catheterization in a case of extremely low birth weight children, with the aim of providing reference for the diagnosis and treatment of such children in clinical settings. Method: A retrospective analysis of the clinical data of secondary necrotizing enterocolitis after the failure of oral ibuprofen closed arterial catheters during hospitalization of 1 case of extremely low birth weight at 25+4 week of gestational age of undergraduate admission was carried out. Results: (1) Male newborns, born prematurely at 25+4 week of gestational age, had an ultrasound on the third day of life: patent ductus arteriosus was not closed (large blood vessel level 2.5mm left-to-right shunt), check body: pre-heart region can be heard and II-III grade contractional murmur, and twice to oral ibuprofen closed PDA failed. Necrotized small intestine colitis occurred during 47 days in hospital, while intestinal fistula, intestinal viscosity relaxation, intestinal torsion reset, intestinal decompression. After 142 days in hospital, the PDA was found to be open again, and more severe than before, and eventually surgical treatment of ligation PDA, after surgery to recover well, 165 days in hospital (corrected gestational age 49 plus 1 week, weight 2600g, milk volume 50ml/Q3h) when improved discharge. Conclusions: PDA is an important factor leading to respiratory dependence, intracranial bleeding, necrotic small intestine colitis, respiratory failure, heart failure and other serious complications in premature babies, and is also one of the main causes of premature death. At present, clinical treatment of PDA with ibuprofen is more common, for drug treatment failure and PDA seriously affect the heart and lung function of children with surgery to close the continuously open arterial catheter.

关键字 Extremely low birth weight infant; necrotizing enterocolitis; patent ductus arteriosus; ibuprofen;

分类：16. Neonatology 新生儿
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Perioperative management of a newborn with spina bifida and meningocele

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Objective: To investigate the perioperative management of a case of spina bifida with meningocele.
Methods: A case of spina bifida with meningocele was retrospectively analyzed to summarize the clinical manifestations, diagnosis, treatment and nursing of the disease. Results: In this case, the patient was admitted to hospital because of ″abnormal spinal development was found in pregnancy for 1 day″. Physical examination on admission showed that the general condition of the newborn was good. There was a cystic mass about 8cm×6cm×5cm on the back, with clear boundary, soft texture, and obvious fluctuation sensation on touch. The transmission test was positive. Bright red skin lesion of 3×3cm on the surface of the mass and no cerebrospinal fluid leakage were observed. The lump increased and the tension increased when the child cried. The operation was performed under general anesthesia on February 7, 2020. After the operation, the newborn recovered well. After 20 days in hospital, the newborn discharged.
Conclusion: The treatment and nursing of children with spina bifida with meningocele is quite difficult. Preoperative treatment of the mass should be cautious, especially care about do not compress, guard against cerebrospinal fluid leakage caused by rupture of the capsule wall, pay attention to the prevention of infection at part of the epidermal ulceration, pay attention to the children's positioning, follow the doctor's advice medication, closely observe the changes of the disease, and cooperate with doctors to arrange and perfect preoperative examination. Postoperative treatments of the spina bifida include observing of anesthesia recovery period, caring incision, positioning, preventing infection, caring drainage tube, and observing the manifestation intracranial infection, acute hydrocephalus, cerebrospinal fluid leakage, and other complications. At the same time, nutritional support, pain control, and guided health education for children's families should also be taken into account.

关键字 spina bifida; Meningingocele; The newborn; perioperative

分类：16. Neonatology 新生儿
1302

A neonate with multisystemic smooth muscle dysfunction syndrome complicated with a window ductus: a case report

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A female term neonate with a birth weight of 3,530 g was admitted to our hospital 11 minutes after birth due to an extremely distended bladder seen on foetal doppler ultrasound. The patient was unable to urinate spontaneously. She experienced bloody stools and tachypnoea six days after admission.
Chest and abdominal radiographs showed increased pulmonary vascularity, enlarged cardiothoracic ratio, and reduced intestinal gas. Echocardiography revealed an 8-mm patent ductus arteriosus (PDA) and brain natriuretic peptide (BNP) values were 50 times higher than normal levels. Doppler ultrasound of the urinary system showed bilateral hydronephrosis, bilateral upper ureteral dilatation, and an excessively distended bladder. The patient also had mydriasis with bilateral 4-mm diameter pupils. Retinal examination revealed retinal vascular tortuosity and multiple dilated arteries near the optic disc. The sagittal and coronal cranial magnetic resonance angiography demonstrated cerebrovascular stiffness.
Surgical ligation of the PDA was conducted at 13-days of age, wherein a 16 mm-large window ductus was found. BNP levels normalised within three days after surgery.
Gene analysis by whole exome sequencing was requested revealing a heterozygous mutation of ACTA2 c. 536 G>A (p. Arg179His), suggesting a pathogenic mutation found in multisystemic smooth muscle dysfunction syndrome.
She was followed-up for three months after discharge and was diagnosed as a low-weight infant with normal motor development but with cognitive delay.

关键字 neonate; multisystemic smooth muscle dysfunction syndrome; window ductus

分类：16. Neonatology 新生儿
1307

The hereditary abnormal fibrinogenemia: a case report and literature review

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Abstract **Objective:** To improve the diagnosis and treatment of hereditary abnormal fibrinogenemia,we analyze the clinical data of a associated case. **Method:** The clinical manifestation, laboratory examination and treatment of a case of hereditary abnormal fibrinogenemia and its family which diagnosed in West China Second Hospital of Sichuan Universityand were analyzed and discussed. **Result:** Combined with the family history, coagulation function and gene detection, which is autosomal dominant or recessive inheritance. And women carrying related genes will have a greater impact on their maternal health and family. **Conclusion：** The clinical manifestations of hereditary abnormal fibrinogenemia are highly heterogeneous, which may not have any clinical symptoms, but may also be manifested as hemorrhage and / or thrombosis. Female patients with pregnancy can cause recurrent abortion and increase the risk of postpartum hemorrhage and thrombosis. The genotype and phenotype of the disease are related, and the diagnosis is mainly based on personal history, family history, abnormal coagulation test and molecular defects. Although there is no need for special treatment for patients without clinical manifestations, it is necessary to be vigilant for female patients who are ready for pregnancy, and make full prenatal diagnosis to avoid complications such as abortion and postpartum coagulation dysfunction.

关键字 Fibrinogen, hereditary abnormality, fibrinogenemia, gene mutation, prenatal diagnosis

分类：16. Neonatology 新生儿
1316

A case of Permanent neonatal diabetes caused by a novel mutation of INS gene and its long-term prognosis

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OBJECTIVE: Neonatal diabetes mellitus (NDM) is a rare form of diabetes, mainly includes two types: transient neonatal diabetes mellitus (TNDM) and permanent neonatal diabetes mellitus (PNDM). Insulin gene (INS) mutations have been described as an important cause of PNDM. The aim of our study is to explore the clinical and genetic characteristics of permanent neonatal diabetes mellitus caused by INS mutations, and to put forward some opinions on treatment and management of this disease.

METHODS: We regularly monitored the patient's blood sugar, the insulin dosage and his growth and development in the past ten years, and we performed a standard 75 g OGTT for the family member and measured plasma glucose, serum insulin, and C-peptide in order to determine whether they have impaired glucose tolerance. The genomic DNA of the patient and his family members was extracted, and the monogenic diabetes-related genes were sequenced.

RESULTS: We describe a patient who was diagnosed in his first day after birth, presenting with low birth weight, progressive hyperglycemia and serious insulin deficiency. A novel homozygous mutation c.1A>G was identified in the patient's INS gene, which is an initiation codon mutation, and there is no same pathogenic literature has been reported before. The genetic linkage study identifies that there are heterozygous carriers in patients' maternal and paternal families. During the ten years, the patient received regular insulin injection. The using time and injected dose were gradually adjusted with the change of the diet and the weight of the patient, and we will describe those changes in detail in the full text. The patient now regularly injects 7 units of ″ insulin Aspart injection ″per day before three meals, and injects 7 units of ″ Insulin detemir″ per day before going to bed. The blood glucose was monitored four times a day, and the blood glucose was well controlled, no acute or chronic complications occurred. Besides, his growth and nervous system development were no difference with the same age.

CONCLUSIONS: We recommend all the NDM patients to confirm the genetic diagnosis as soon as possible, which is really important for the follow-up treatment and the judgment of long-term prognosis. The genetic diagnosis results of the patients' family members should also attract enough attention, on account of they are more susceptible to develop diabetes than ordinary ones. Although none of the heterozygous carriers in the patient family in our study showed impaired glucose tolerance or decreased insulin production, long-term blood glucose monitoring is of great significance to their health management. At the same time, all examinations related to common complications of neonatal diabetes, such as retinopathy, abnormal renal function, peripheral neuropathy and mental retardation, were negative for our patient. Therefore, early using of insulin and continuous blood glucose monitoring for the INS mutation patients are necessary for their long-term prognosis, although this is a process that requires great patience. In general, this NDM case with a full 10-year follow-up and good prognosis is particularly valuable, we should continue to follow him and his family closely.

关键字 Homozygosity; INS gene; Neonatal diabetes; Follow-up

分类：16. Neonatology 新生儿
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The role of fecal calprotectin in the diagnosis of neonatal necrotizing enterocolitis: A systematic review and meta-analysis

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Background Fecal calprotectin has been extensively investigated as a detection marker for necrotizing enterocolitis (NEC). However, there is no current consensus regarding its effectiveness as a diagnostic test.
Objective To evaluate the effectiveness of fecal calprotectin as a detection marker for NEC.
Design We conducted a systematic review of studies published in PubMed, Embase, and the Cochrane Library from 2005 to 2020. Studies based on PICOS were included in this systematic review.
Results Twelve studies, which had 683 neonates were included in this study. The studies analyzed over 3000 stool samples. Heterogeneity was significant (I^2 = 56.2%, P = 0.009), hence, a randomized-effects model was used for the analysis. The combined sensitivity and specificity were 0.91(95% CI: 0.83-0.95) and 0.91(95% CI: 0.79-0.96), respectively. The AUC was 0.96 (95% CI: 0.94-0.97). However, publication bias (Begg's test P = 0.003) was observed. Meta-regression analysis showed that the P-value of Design before and after adjustment was significant (P<0.05), suggesting that the Design was the cause of heterogeneity. Conclusion The clinical diagnostic value of fecal calprotectin for NEC was good.

关键字 fecal calprotectin; biomarkers; necrotizing enterocolitis.

分类：16. Neonatology 新生儿
1334

Contents of human milk oligosaccharides (HMOs) in breast milk of mothers delivering preterm infants of different gestational ages and their effects on early growth and development

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Objective To investigate the human milk oligosaccharides (HMOs) contents in breast milk of mothers delivering preterm infants and their effects on the early growth and development of infants. Methods In this prospective cohort study, full-term and preterm newborns whose parents decided to breastfeed were recruited from Peking University Third Hospital between December 1, 2017 and November 30, 2018. The preterm infants were divided based on their gestational ages into extremely preterm (<28 weeks), very preterm (28-31+6 weeks) and moderate to late preterm (32-36+6 weeks) groups. Breast milk was collected from mothers at 7, 14, 28 and 120d postpartum. 368 breast milk samples were collected from 125 mothers in this study, including 54 mothers of full-term infants, 23 mothers of moderate to late preterm infants, 39 mothers of very preterm infants, and 9 mothers of extremely preterm infants. Ultra-performance liquid chromatography-mass spectrometer (UPLC-MS/MS) was used to determine the concentration of 2'-fucosyllactose (2'FL), 3-fucosyllactose (3FL), 3'-sialyllactose (3'SL), A-tetrasaccharide (P1), lacto-N-tetraose (LNT), lacto-N-neotetraose (LNnT), lacto-N-fucopentaose II (LNFP-II) and lacto-N-fucopentaose V (LNFP-V). Secretor status of mothers was defined as 2'FL concentration in colostrum and transitional milk greater than 200μg/mL. Weight gain and the occurrence of allergic diseases of infants were collected at 120d (4 months) postpartum. The chi-square test or the Fisher's exact test was used for the comparison of categorical data between groups; Kruskal-Wallis test and Wilcoxon rank sum test were used for comparison of continuous data between groups. Nemenyi test was used for multiple comparison. Results 79.2% (99/125) of the mothers were secretor. There were no statistical differences between groups in the secretor status of mothers (χ^2=1.31, P>0.05). The total concentration of HMOs peaked at 1-2 weeks postpartum. Compared to the preterm milk, the HMOs from the term milk was trending downwards at an earlier time. In the breast milk of secretor mothers on 28d, total concentration of HMOs significant differed among the three groups of preterm milk and the term milk, with the median value of 4587.09，4615.25，5277.44，5476.03 μg/mL, respectively (Kruskal-Wallis χ^2 = 8.1234，P=0.044). 3. When analyzed by the median weight gain of the infants (low vs high weight gain) at 4 months postpartum, 2'FL was significantly lower in the high weight gain group at 7 d (1818.04μg/mL vs 2181.67 μg/mL, W = 1386，P=0.018), while LNT & LNnT were significantly higher (1182.36μg/mL vs 1053.62 μg/mL, W = 816，P=0.044). 4. The level of 3FL at 120 d was significantly affected by presence of allergic disease in infants, breast milk from mothers of infants with allergic disease had lower 3FL than those from mothers of infants without allergic disease (256.17μg/mL vs 286.18 μg/mL, W = 564，P=0.026). Conclusions The overall profiles of HMOs in breast milk of mothers delivering preterm infants was basically the same as that of mothers delivering term infants; individual HMOs play a role in weight gain and the development of allergic diseases in preterm infants, but the mechanism is unclear and needs further study.

关键字 Human milk oligosaccharides; Preterm; Weight gain

分类：16. Neonatology 新生儿
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Metformin induces M2 macrophage polarization through Shh signaling to improve lung vascular development in bronchopulmonary dysplasia

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Metformin has potential anti-inflammatory properties and accelerates wound healing through enhancing vascular development. This study aimed to investigate the effects and mechanisms of metformin on pulmonary vascular development. Newborn mice were subcutaneously injected with metformin from the second day after exposure to hyperoxia. Pulmonary vascular development, inflammation, and the expression of Shh signaling pathway proteins were evaluated using western blotting and immunofluorescence staining. M2 macrophage polarization was measured using flow cytometry. The effect of metformin in macrophage polarization was revealed using RAW264.7 macrophages exposed to 90% oxygen in vitro. The role of metformin and purmorphamine on M1 macrophages and M2 polarization was observed using flow cytometry. Hyperoxia decreased pulmonary M2 polarization and metformin increased the number of M2 macrophages after hyperoxic exposure on postnatal day 14. Metformin enhanced CD31 expression and suppressed inflammation in the lung of mice exposed to hyperoxia on postnatal day 7 and 14. Metformin decreased Gli1 expression in pulmonary macrophages in the lung after exposure to hyperoxia on postnatal day 14. Metformin decreased Gli1 expression in RAW264.7 macrophages exposed to 90% oxygen, which was reversed after purmorphaminepretreatment. Exposure to 90% oxygen restrained the polarization of M2 macrophages; metformin enhanced the number of M2 macrophages. Purmorphamine reversed the effects of metformin on M2 polarization in RAW264.7 macrophages exposed to hyperoxia. In conclusion, these results may indicate that metformin induces the polarization of M2 macrophage by downregulating the Shh signaling pathway to improve pulmonary vascular development in bronchopulmonary dysplasia.

关键字 BPD, metformin, macrophages, vascular development, Shh signaling pathway

分类：16. Neonatology 新生儿
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The evaluation of antimicrobial stewardship for bacterial meningitis in neonates: a retrospective cohort study.

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To compare the efficacy and safety among neonates suffering from bacterial meningitis (BM) of a relatively shortened duration of antibiotic treatment compared to the currently recommended course.
A retrospective noninferiority cohort study of the relatively shortened antibiotic duration versus the currently recommended antibiotic strategy in the neonates (gestational age (GA) or corrected GA≥35 weeks) diagnosed with BM was performed.

关键字 neonate, bacterial meningitis, antimicrobial stewardship

分类：16. Neonatology 新生儿
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Implementation experience of a 12-month intervention to introduce intermittent kangaroo mother care to eight Chinese neonatal intensive care units

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Background
Kangaroo mother care (KMC) is recommended by the WHO for the care of preterm and low birth weight newborns, in China it is an under-utilized intervention that could improve the management and outcomes of preterm and low birth weight infants.

Methods
This was a multicenter study conducted in the NICUs of eight hospitals in China, between April 2018 and March 2019. We collected and compared the service capacity of study NICUs at the start and end of the implementation period. Additional data was collected for infants who received KMC including the number of times they received KMC and the length of time KMC was provided, infants who received KMC in the NICUs were followed up post discharge at 40-41 weeks CGA to determine if they were still receiving KMC and weight gain.

Results
The average number of KMC lounge chairs per NICU increased from 7.5 in March 2018 to 10.6 in March 2019, the average number of nurses that received KMC training per NICU increased from 61.9 to 67.1, and the number of nurses that could perform KMC increased from 23.1 to 43.3. A total of 8240 infants were enrolled in eight study NICUs and 2093 (25.4%) received KMC. For preterm infants who received KMC, 49.6% of them had a GA at birth between 28-32 weeks and 41.9% had a birth weight between 1000-1500g. The percentage of infants who received KMC that continued to receive KMC post-discharge increased from 33.7% to 65.8% over the 12-month period. On average infants who continued to receive KMC post discharge received it once a day for just under an hour.

Conclusions
Around one-quarter of all preterm infants admitted to the NICU received KMC, those with a lower birth weight were more likely to receive KMC than heavier babies and those with a greater GA. The proportion of preterm infants that received KMC did not change over the 12-month period despite the increase in units' service capacity. We recommend a more in-depth study of hospital context, process and additional resources required in order for KMC to be further scaled up in China's NICUs

关键字 Kangaroo mother care; China; Implementation experience; Service capacity; NICUs

分类：16. Neonatology 新生儿
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Analysis of changes of clinical characteristics of neonatal pneumothorax over 11 years

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Objective: To investigate the etiology and clinical characteristics of neonatal pneumothorax, and to provide useful information for clinical treatment of neonatal pneumothorax.
Methods: A total of 104 cases of neonatal pneumothorax hospitalized in the Department of Pediatrics of Peking University Third Hospital from January 1, 2010 to December 31, 2020 were selected as subjects. Clinical data related to neonatal pneumothorax were retrospectively studied and grouped. According to the length of hospitalization, the children were divided into two groups: ① the first 6 years: 42 patients from January 1, 2010 to December 31, 2015; ② the last 5 years: 62 cases from January 1, 2016 to December 31, 2020. According to the gestational age, they were divided into: ① full term infants group: 42 cases of gestational age ≥37 weeks; ② premature infants group: 62 cases of gestational age < 37 weeks. SPSS software was used for statistical analysis.
Results: 1. Characteristics of pneumothorax: the incidence of pneumothorax was 0.76% (104/13620), and male children accounted for 64.4% (67/104). The average gestational age at birth was 35+4 weeks, and the average birth weight was 2585.7g. The mean hospital stay was 14.4 days. The average postnatal age of pneumothorax was 29h, and the occurrence of pneumothorax within 24h (≤24h) accounted for 59.6% (62/104), within 24h ~ 48h accounted for 32.7%, > 48h accounted for 7.7%. 61.5% pneumothorax occurred on the right side, 26.0% on the left side and 12.5% on both sides. Mediastinal emphysema was found in 8 cases, subcutaneous emphysema in 8 cases, and pulmonary interstitial emphysema in 2 cases. 17 cases (16.3%) were spontaneous pneumothorax. Wet lung was the primary disease in 37.5%. 26% had used surfactant (PS) before pneumothorax developed. The amount of pneumothorax <30% accounted for 46.2%, 30% ~ 70% accounted for 49.0%, 5 cases (4.8%) pneumothorax > 70%. There were statistically significant differences between non-invasive mechanical ventilation and invasive mechanical ventilation before and after pneumothorax (P < 0.05). After pneumothorax occurred, 39% were treated conservatively, 13% were treated by puncture alone, and 48% were treated by puncture combined with closed thoracic drainage. 96.2% of the enrolled children were discharged from hospital after clinical recovery, and 4 cases died. 2. The incidence of pneumothorax in the first 6 years and the last 5 years was 0.63% and 0.90%, respectively, with an increasing trend year by year (P=0.07). The proportion of thoracic closed drainage in the last 5 years was higher than that in the first 6 years, and the difference was statistically significant (P < 0.05). 3. The incidence of pneumothorax in premature infants was higher than that in full-term infants (1.02% and 0.56%, respectively), with statistical significance (P < 0.05). Compared with preterm infants, the occurrence of pneumothorax in term infants was more concentrated within 24h after birth, and the preterm infants had more closed thoracic drainage than only puncture treatment or conservative treatment, with statistical significance (P < 0.05).
Conclusion: The incidence of neonatal pneumothorax has an increasing trend, premature infants are more than full-term infants, most of them occur within 24 hours after birth, mostly on the right side, the amount of pneumothorax is mainly small to medium,

and invasive mechanical ventilation is mostly used after pneumothorax occurs., Closed thoracic drainage is an effective treatment to neonatal pneumothorax.

关键字 newborn; pneumothorax; change features

分类：16. Neonatology 新生儿

1411

Analysis of the clinical characteristics of neonatal hemolytic disease of rare blood group incompatibility

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Objective Hemolytic disease of the newborn specifically refers to the neonatal homoimmune hemolytic disease caused by the incompatibility of maternal and infant blood types. Rare blood group incompatibility, although it is often used as the cause of neonatal jaundice and anemia for differential diagnosis, requires special laboratory tests to confirm the diagnosis, which is easy to be missed and often delayed in treatment. In severe cases, it leads to poor prognosis. Therefore, this study took ABO blood group incompatibility hemolytic disease as a control, retrospectively analyzed the clinical characteristics of the rare blood group incompatibility HDN in our hospital, and further understood the clinical characteristics of the rare blood group incompatibility HDN, in order to achieve early diagnosis and treatment of such diseases and improve the prognosis of newborns. Purpose.

Methods Patients who were hospitalized in the neonatal intensive care unit and neonatal ward of Peking University Third Hospital from June 1, 2009 to December 31, 2020 and were clearly diagnosed as neonatal hemolytic disease (including ABO hemolytic disease, RH Children with blood group incompatibility hemolytic disease and other rare hemolytic diseases caused by blood group incompatibility are the subjects of the study. According to the different red blood cell antibodies, the research subjects were divided into the following two groups: ①Common blood group incompatibility: children with ABO blood group incompatibility hemolytic disease; ②Rare blood group incompatibility: RH blood group incompatibility hemolytic disease or other rare blood group incompatibility hemolytic disease Children with RH blood group incompatibility are divided into RHD group (hemolysis induced by RH anti-D antibody) and non-RHD group (by RH anti-c, anti-C, anti-E, anti-e Antibody-induced hemolysis). There were 28 rare cases of blood group incompatibility, and they were born according to a 1:3 ratio. 84 newborns with similar gestational age (±2w), similar birth weight (±200g), hospitalization during the same period (±2w) and a clear diagnosis of ABO blood group incompatibility hemolytic disease were used as controls, and their general information, clinical manifestations, and experiments were analyzed and compared Laboratory examination, treatment and outcome.

Results Compared with ABO blood type incompatibility, hemolytic disease caused by rare blood type had earlier appearance of jaundice, a higher proportion of combined hepatosplenomegaly and anemia, more severe anemia, and earlier occurrence. Rarely, hemolytic disease caused by blood group incompatibility has a higher positive rate of direct anti-human ball test, and a greater proportion of patients need to receive treatments such as strong light therapy, IVIG, blood transfusion and transfusion. In hemolytic diseases caused by RH blood group incompatibility, hemolysis induced by RH anti-D is more severe than hemolytic anemia induced by RH anti-C, anti-c, anti-E, and anti-e antibodies, and the proportion of hepatosplenomegaly is higher. High, jaundice lasts longer, and the proportion of receiving IVIG and strong light therapy is higher.

Conclusion Hemolytic disease of the newborn is an important cause threatening the health and life of newborns. It can not only cause severe anemia and hypercholesterolemia in the early birth of newborns, but anemia may continue throughout the neonatal period or even the first year of life. First of all, during pregnancy, attention should be paid to the monitoring of irregular red blood cell

antibodies, and follow-up of those who are positive for irregular red blood cells should be strengthened. Secondly, in terms of laboratory tests, except for the RH blood type, the positive rate of DAT for other blood types incompatibility is low. It is recommended to make a comprehensive diagnosis based on the clinical manifestations and IAT results to avoid missed diagnosis.

关键字 neonatal hemolytic disease of rare blood group incompatibility; ABO; Newborn

分类：16. Neonatology 新生儿

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The application of EEG/NIRS multimodality monitoring on neonatal encephalopathy using neurovascular coupling

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Background: Neonatal encephalopathy is a serious disease that affects the early survival and long-term neurodevelopmental prognosis of the infants. Amplitude-integrated electroencephalography (aEEG) monitors neuronal electric activity, while near infrared spectroscopy (NIRS) reflects changes in cerebral tissue oxygenation (rSO2). Neurovascular coupling (NVC) refers to the physiological connection between neuronal electric activity and the immediate change in local cerebral blood flow, which can be quantitatively detected through multimodalities of EEG/NIRS coupling. In this study, the bedside combined aEEG/NIRS multimodality monitoring quantitatively analyzed the strength of NVC, and searched for sensitive markers for the diagnosis and prognostic prediction of neonatal encephalopathy.

Method: Neonates at risk for neonatal encephalopathy admitted to Peking University First Hospital were recruited, and the simultaneous monitoring of aEEG and NIRS was carried out for 6 hours after birth. Through the interdisciplinary research of clinical and biomedical engineering, the strength of NVC was calculated. The included neonates at high risk of encephalopathy were clinically allocated into groups without encephalopathy, with mild encephalopathy, and severe encephalopathy. First, we explored the association of NVC strength within different frequencies (0.0025-0.015Hz, 0.001-0.0025Hz, 0.0001-0.001Hz) with clinical diagnosis. Then, neonates were followed up to 6-18 months to assess the neurodevelopmental prognosis and explore the predictive value of the strength of NVC in the neonatal period on neurodevelopmental outcome.

Results: A total of 96 newborns at risk for encephalopathy were included in this study. Clinically, they were divided into 42 cases without encephalopathy, 47 with mild encephalopathy, and 7 with severe encephalopathy.

1. Association of NVC strength with diagnosis

(1) Within 0.0025-0.015 Hz, NVC strength of neonates with mild encephalopathy (0.399±0.093) were 11.5% lower than those without encephalopathy (0.451±0.093) (P=0.011), and NVC strength of neonates with severe encephalopathy (0.328±0.116) were 27.3% lower than those without encephalopathy (P=0.003).

(2) Within 0.0001-0.001 Hz, NVC strength of neonates with mild encephalopathy (0.472±0.159) was 24.9% higher than those without encephalopathy (0.378±0.170, P=0.0087), while NVC strength of neonates with severe encephalopathy (0.218±0.177) was 42.3% lower than those without encephalopathy (P=0.027).

(3) Within 0.001-0.0025 Hz, there was no significant difference among the groups.

2. Association of NVC strength with 6-18 month neurodevelopmental outcome

Among 54 neonates with encephalopathy, 41 had a normal neurodevelopmental prognosis at 6-18 months, and 13 had neurodevelopmental delay.

(1) Within 0.0001-0.001Hz, NVC strength of neonates with developmental delay (0.285±0.157) was 41.6% lower than those with normal prognosis (0.488±0.162) (P=0.0002), with a prognostic sensitivity of 75.6%, and a specificity of 76.9%. aEEG alone had a sensitivity of 69.2% and a specificity of 65.9%.

(2) Within 0.0025-0.015 Hz and 0.001-0.0025 Hz of the coupling strength, there was no difference in NVC strength between neonates with normal and delayed neurodevelopmental outcome.

Conclusions: In neonates with mild neonatal encephalopathy (mild HIE and mild intracranial hemorrhage), the diminishing of NVC in the frequency of 0.0025-0.015Hz may be a sensitive marker for detecting of brain injury. The enhancing of NVC in the frequency of 0.0001-0.001Hz may reflect compensation of function. In neonates with severe neonatal encephalopathy (severe intracranial hemorrhage), NVC strength was diminished within 0.0001-0.001Hz, indicating the severity of brain injury. In all neonates with encephalopathy, NVC strength within 0.0001-0.001Hz was a sensitive predictive marker of neurological outcome at 6-18 months of age, its predictive sensitivity surpassed that of aEEG alone.

关键字 aEEG, NIRS, neonatal encephalopathy, neurovascular coupling, prognosis

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Risk factors of eosinophilia in low birth weight infants

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【Abstract】【Objective】Analysis of factors influencing eosinophilia in low birth weight infants. 【Methods】A case-control study was used to divide into eosinophilia group (150 cases) and control group (150 cases) according to whether eosinophilia was present or not. Identified by univariate analysis, and followed by unconditional logistic regression analysis of factors influencing eosinophilia in low-birth-weight infants. Comparison of eosinophils at different times after birth of children whose mothers had and did not have gestational hypertension. Comparison of eosinophils difference in children with postnatal infections, BPD, and food allergies at different times before and after the onset of corresponding symptoms. 【Results】1. Eosinophils in both groups peaked in the third week after birth and then gradually declined, but a longer duration of eosinophilia showed in the eosinophilia group. 2. The case number of mothers with gestational hypertension, premature rupture of membranes, postnatal food allergy, infection, anemia, blood transfusion, and BPD in both groups was respectively 59 (39.3%) vs 33 (22.0%), 47 (31.3%) vs31 (20.7%) ; 10 (6.7%) vs1 (0.7%) ; 54 (36.0%) vs15 (10.0%) ; 133 (88.7%) vs88 (58.7%) ; 67 (44.7%) vs26 (17.3%) ; 75 (50.0%) vs23 (15.3%) , and the difference was statistically significant (χ2=10.598、4.435、7.644、28.628、34.796、26.196、40.978; P=0.001、0.035、0.006、0.000、0.000、0.000、0.000) . Platelets of both groups were respectively 323.5 (71,660) ×109/L and 294.5 (90,515) ×109/L, and the difference was statistically significant(Z=-3.183P=0.001). 3. Unconditional logistic regression analysis showed that mothers' gestational hypertension, infection, BPD, food allergy, and platelet level were factors influencing eosinophilia in low- birth-weight infants(OR=3.982、3.832、4.617、14.246、1.007; 95%CI =1.995-7.947、1.739-8.448、2.326-9.162、1.581-128.322、1.003-1.010). 4. The eosinophils of children on the day of birth whose mothers had and did not have gestational hypertension were respectively 0.10 (0.00, 0.70) ×109/Land 0.08 (0.00, 0.68) ×109/L, and the difference was statistically significant(Z=-2.504,P=0.012).5. Eosinophils were respectively 0.32 (0.01,2.6)×109/L on the day of the onset of infection and 0.91 (0.02,3.1) ×109/L after 3 days, with a statistically significant difference (adjusted P < 0.05).6. Eosinophils in children with BPD were 0.09 (0.00,2.50)×109/L on the day of birth, 0.23 (0.00,3.95)×109/L after 3 days, and 0.89 (0.02,6.1)×109/L after 3 weeks, with statistically significant differences (adjusted P < 0.05).7. Eosinophils in children with food allergy were 0.43 (0.21,2.12)×109/L on the day of birth and 1.07 (0.48,3.68)×109/L on the day of the onset of allergy, with statistically significant differences (adjusted P < 0.05). 【Conclusions】For this group, mothers' gestational hypertension, infection, BPD, food allergy, and platelet increasement were factors influencing eosinophilia in low-birth-weight infants.

关键字 Infant, low birth weight; Eosinophilia; Risk factors

分类：16. Neonatology 新生儿
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Clinical characteristics of peripherally inserted central venous catheter related venous thrombosis in preterm infants

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Objective:To investigate the clinical characteristics and risk factors of venous thrombosis associated with peripherally inserted central catheters (PICC) in preterm infants.
Methods:We found seven premature infants with PICC related venous thrombosis hospitalized in the pediatric neonatal intensive care unit (NICU) of the Peking University Third Hospital from January 1, 1994 to June 30, 2021. They were defined as the thrombosis group. At the same time, they were matched 28 premature infants who received PICC catheterization according to the ratio of 1:4 with similar gestational age (± 2W), birth weight (± 200g) and the same period (± 2W) as the control group, who were defined as the non-thrombotic group. The clinical information of the two groups was collected through the hospital electronic medical record system. SPSS statistical software was used for comparison between the two groups.
Results:1. There was no statistical significance in birth weight, gestational age and gender composition between thrombosis group and non-thrombosis group (P > 0.05). 2. Univariate analysis showed that compared with non thrombosis group, the mothers of neonates in thrombosis group were complicated with autoimmune diseases during pregnancy (F=10.9, P = 0.002) , thrombocytopenia (F= 4.6, P = 0.04), sepsis (F=5.1, P = 0.04) and cardiac insufficiency (F=4.6, P = 0.04) were more likely to occur in neonates with thrombosis. 3. In the thrombus group, the time from catheterization to thrombus was 1-36 days. 85.7% (6 / 7) neonates were deep venous thrombosis. 3 cases occurred within 2 days after central venous catheter extubation, 4 cases occurred during central venous catheter indwelling, and 4 cases were in lower limb veins. The clinical manifestations of thrombosis were skin edema and cyanoze and skin temperature changed of affected limbs. The coagulation function indexes of 7 patients were normal when thrombus was diagnosed, and D-dimer has a significant increase1-2 days after thrombosis.5-7days it fell back to the normal level. All 7 neonates were treated with Low-Molecular-Weight Heparin Sodium Injection to anticoagulate for 3-17 days.All 7 neonates recovered completely.
Conclusion: PICC related thrombosis occurs within 1 week after PICC catheterization. It is more likely to occur when the mother has autoimmune diseases, the child has thrombocytopenia, sepsis and cardiac insufficiency. When there are the above high-risk factors and the child has swelling in the limbs after PICC catheterization for 1 week, vessel ultrasound should be performed immediately for timely diagnosis and treatment, so as to reduce the risk of adverse complications.

关键字 premature infants,peripherally inserted central catheters (PICC),thrombosis

分类：16. Neonatology 新生儿
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The role of ADMA and ARG-2 in intrauterine growth restriction-related vascular endothelial dysfunction

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Objective: Intrauterine growth restriction (IUGR) is an important risk factor for stillbirth and neonatal complications, which significantly increases perinatal morbidity and mortality. The purpose of this study was to investigate the potential molecular mechanisms of IUGR-related vascular endothelial dysfunction.
Methods: Human umbilical vein endothelial cells (HUVECs) were separated from fresh umbilical cord tissues collected from appropriate for gestational age (as control) and IUGR newborns. The bioavailability of asymmetric dimethylarginine (ADMA) and expression of arginase-2 (Arg-2) was analyzed.
Results: In this study, 15 cases respectively were enrolled in the IUGR group and the control group. The results showed that NO production was reduced in HUVECs in the IUGR group compared with the control group ($P < 0.01$). At the same time, eNOS expression was decreased ($P < 0.05$), and activity of arginase ($P < 0.05$) and the expression level of ARG-2 ($P < 0.01$) was increased. In addition, level of ADMA ($P = 0.001$) and ADMA/L-Arginine ratio ($P < 0.05$) was increased. The expression of dimethylarginine dimethylaminohydrolase (DDAH1) was significantly decreased ($P = 0.01$). Under low oxygen conditions, the ADMA/L-Arginine ratio in HUVECs of the IUGR group was substantially increased ($P < 0.01$). Meanwhile, the expression of protein arginine methyltransferase 1 (PRMT1) was significantly increased ($P < 0.01$).
Conclusion: This study shows that the activation of ARG-2 and the accumulation of ADMA plays an important role in IUGR-related vascular endothelial dysfunction. The study provides experimental evidence for the fetal developmental origin of cardiovascular disease at the cellular level.

关键字 intrauterine growth restriction, vascular endothelial dysfunction

分类：16. Neonatology 新生儿
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Current status of the application of docosahexaenoicacid in neonates in the past five years

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Objective: To investigate the current status of the application of docosahexaenoicacid (DHA) in neonates in the past five years, and to describe the trend of research in the field.
Methods: PubMed was searched for English articles published in the past five years (2015-2019), with the combination of key words and MeSH terms. The articles were screened according to inclusion and exclusion criteria.
Results: The results showed that DHA was mainly studied in two aspects of the clinical practice. On the one hand, the benefits for newborns were explored when DHA supplementation was given during pregnancy or lactation period. On the other hand, DHA attracted wide attention as a clinical examination for specific neonatal diseases and a tool for prognostic evaluation.
Conclusions: As a critical nutrient for the formation and function of the nervous system, DHA has received increasing attention in the recent years. However, more research is needed to explore how to maximize the benefits of DHA.

关键字 docosahexaenoicacid , neonate

分类：16. Neonatology 新生儿
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The incidence and outcome of neonate in early onset urea cycle disorders—review and meta-analysis of 3514 patients

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Background：Urea Cycle disorders (UCD) is a common metabolic disorder in children.Severe urea cycle disorders often lead to irreversible neurological damage or even death due to hyperamemia. However, the incidence and prognosis of early-onset UCD(EO) in neonates are highly heterogeneous in different clinical studies.The main purpose of this study was to explore the incidence of EO in urea cycle disorders and the incidence and prognosis of different types of UCD in the neonatal period, and try to provide some useful evidence for future diagnosis and treatment.
Methods：MEDLINE , EMBASE, Cochrane and Chinese Biological Medicine databases were searched from 1978 until July 2021 using the Medical Subject Heading (Mesh) terms.Proportions and prognosis of EO were analyzed with a random effects model.intervals Effects of publication year and geographic area were analysed by meta-regression.
Results: We included a total of 29 clinical studies about early-onset and late-onset urea cycle disorders in the end, including 18 (62%) published before 2010 and 11 (38%) published after 2010.Of the 29 studies, 3 were from Europe, 2 from Italy, 2 from Spain, 2 from Turkey, 7 from the United States, 4 from Japan, 1 from the common Cohort of Europe and the United States, 1 unspecified, and the rest were from Finland, France, Germany, India, Mexico.A total of 3,514 UCD patients were enrolled in 29 studies, including 1,743 patients who developed UCD in the neonatal period，the overall incidence of EO was 49.6%.In early-onset UCD.Proportions for EO manifestation from high to low were: CPS1D, OTCDm, OTCDf, ASSD and ASLD.
Conclusion：UCDs, have high risks of EO disease manifestation and OTC has a relatively good prognosis. It may provide a comprehensive description of the natural history of EO UCDs，and provide some clue to Clinical practice and scientific research for clinicians and scientists.

关键字 early onset urea cycle disorders ; meta-analysis; incidence ; outcome

分类：16. Neonatology 新生儿
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Role of SHED transplantation in the regulation of HMGB1 in neonatal rats with Hypoxic-ischemic

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Background: To explore role of SHED transplantation in the regulation of HMGB1 in neonatal rats with Hypoxic-ischemic.
Method: Postnatal day 3 SD neonatal rats were divided into Sham group, HI group and SHED group. HI group rats were carried out the ligation of right common carotid artery under the condition of inhalation anesthesia of isoflurane, and then exposed to the hypoxia environment (6.0% oxygen) for 2h. Sham group rats were just separated the right common carotid artery, but without the ligation and hypoxia operation. SHED group then carried out the intracerebroventricular injection of the SHED after 24h of HI. To detect pathological changes of rats, brain tissues were collected at 2d after setting models. Western blot and Immunofluorescence were used to detect the level of IL-1β、IL-10 , BDNF and HMGB1 in the cytoplasm at 2d after setting models.
Results: H&E results showed that appearance of the cells was edema and tissue structure was loose in HI group after 2d of modeling. Immunofluorescence showed that compared to the Sham group, level of IL-1β and HMGB1 in the cytoplasm increased significantly at 2d after HI operation ($P < 0.05$) , however, level of IL-10 and BDNF showed the opposite trend. After SHED transplantation, level of IL-1β and HMGB1 in the cytoplasm decreased significantly at 2d after setting model, but the expression of IL-10 and BDNF increased compared to the HI group.
Conclusions: Role of SHED transplantation may regulate the expression of BDNF and cytokines to regulate HMGB1 translocation in neonatal rats with Hypoxic-ischemic.

关键字 SHED，HMGB1，Hypoxic-ischemic

分类：16. Neonatology 新生儿
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Amniotic fluid stem cells for the treatment of neonatal diseases

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Background:
Cell therapy is an important and promising branch of regenerative medicine, with valuable experience gained in both preclinical research and clinical trials over the past decade. A variety of stem cells have been proposed for the treatment of diseases affecting neonates. Compared with embryonic stem cells (ESC) and adult stem cells (ASC) , amniotic fluid stem cells (AFS) not only can be easily obtained but also are safe to the pregnant women and her fetus. Meanwhile, the isolated and amplified AFS have some surface markers as same as other stem cells and call differentiate into many cells, such as respiratory epithelium, chondrocytes, adipocytes, neural cells, and endothelial cells. AFS genetically originate from the fetus itself, thereby can be used in autologous transplantation without concern for immunologic rejection of donor cells upon delivery. This review discusses the latest development of AFS and applications in neonatal disease.
Methods:
The recent articles about AFS were extensively reviewed. The most common neonatal diseases as well as future application of AFS were summarized and discussed.
Results:
Stem cell therapy has shown to be an effective way of treating neonatal diseases, such as necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), hypoxic-ischemic encephalopathy (HIE) and myelomeningocele (MMC), diseases that continue to be the cause of morbidity and mortality among neonates.
Conclusion:
AFS treatment does not raise ethical issues, can be collected during pregnancy and prepared in sufficient numbers for therapeutic use. In recent years, the therapeutic effects of AFS on neonatal diseases have become evident. This review discusses the efficacy of AFS therapy in preclinical studies to date and their potential applications to diseases that afflict many infants. As a new stem cell, the major hurdles that must be overcome before cell therapies can be safely used in the neonatal intensive care unit.

关键字 amniotic fluid stem cells (AFS), neonatal diseases

分类：16. Neonatology 新生儿
1543

To compare the effects of donor breast milk before and after use on the short-term outcomes of very low birth weight infants

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Objective: To compare the short-term outcomes of VLBW premature infants fed with donor breast milk after the establishment of pediatric breast milk bank in our hospital and those fed with formula milk before.
Methods: Retrospective cohort study 40 extremely low birth weight premature infants admitted to our hospital from October 2017 to March 2019 and 51 extremely low birth weight infants admitted to our hospital from April 2019 to September 2020. The former infants were fed with formula and maternal breast milk, while the latter infants were fed with donor breast milk and maternal breast milk. The differences in short-term clinical outcomes during hospitalization were compared between the two groups.
Results: There were no significant differences in sex ratio, gestational age, birth weight, delivery mode and maternal delivery age between the two groups. The gestational age and weight were 205.2±14.8 days and 207.5±15.5 days, 1176.4±216.1g and 1154.7±246.5g, respectively. There were no significant differences between the two groups in terms of time to regain birth weight, time to start breast-feeding, time to add breast milk fortifier, weight at discharge, body length, head circumference, duration of non-invasive ventilator use, length of hospital stay, incidence of NEC, ROP and BPD. There were significant differences between the two groups on the 14th day after birth in the amount of enteral feeding and the time when the amount of enteral feeding reached 120ml/kg and 150ml/kg, which were 81.0± 41.8mL vs 108.2± 53.1mL, P =0.02, respectively. 30.0±12.0 days vs 17.5±10.2 days, P <0.001, 32.3±11.9 days vs 22.1±13.3 days, P =0.001. There were significant differences in the number and days of use of percutaneous central venous catheterization (PICC) between the two groups (40 cases (100%) vs 30 cases (58.8%), P <0.001, 31.4±2.7 days vs 16.4±2.1 days, P <0.001). There were significant differences between the two groups in the number of patients with advanced sepsis (50%) and the number of red blood cell infusion (23.5%), which were 20 cases (50%) and 12 cases (23.5%), P =0.011, 2.4±0.3 times vs 0.9±0.2 times, P <0.001.
Conclusion: China's domestic breast milk banks were established in Guangzhou in 2013, but there are few studies on the use of donated breast milk for premature infants. There are no data on donated breast milk for very low birth-weight preterm infants in Beijing. The clinical observation of our hospital for 18 months after the establishment of the breast milk bank found that donor breast milk can significantly reduce the incidence of feeding intolerance, greatly improve the rate of enteral nutritional feeding, thereby reducing the utilization rate of PICC, significantly reduce the incidence of advanced sepsis in the hospital, and reduce the use of blood products. So can reduce premature nosocomial infection risk, reduce the economic costs caused by the infection, reduce the risk of blood products use cause, as a mother enough milk a premature infant formula has obvious advantages, at the same time foreign data show that breastfeeding is donated formula feeding may in the short term growth index growth is poorer, but this research did not find the difference. At the same time, it was observed that donor breastfeeding did not reduce the incidence of NEC and other premature complications, nor did it significantly shorten the length of hospital stay. Considering the low incidence of NEC in our hospital in the past, we believe that there may be multiple factors involved in the occurrence of NEC,

among which feeding mode is only one factor. Therefore, general management of NEC may be more meaningful to reduce its incidence. In conclusion, donor breast milk rather than formula milk is recommended for very low birth weight babies when maternal breast milk is not available.

关键字 human milk bank donor human milk very low body weight

分类：16. Neonatology 新生儿

1774

Successful treatment of a case of candida glabrata meningitis with combination of amphotericin B-flucytosine therapy

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AIM: Candida meningitis is exceedingly rare and is usually caused by C. albicans. But the experience in combination of amphotericin B-flucytosine therapy in preterm infants is limited. The aim of this study the efficacy and safety of flucytosine in the treatment of candidiasis in a preterm infant

Method A case of preterm infant with candida glabrata meningitis treated with amphotericin B combined with flucytosine was analyzed

Result：Male infant, gravida 2, para 2. The twins were delivered with emergency caesarian section due to fetal distress. Amniotic fluid was clear. There was no premature rupture of membrane. The first twin was born at 29+6 weeks of gestation. The body weight was 1.7kg and the Apgar score was 5, 8 and 9 at 1, 5 and 10 minutes. At birth, he showed no respiratory effort, bradycardia and generalized cyanosis, so he was resuscitated with intubation in the delivery room. Ventilatory support continued after admission. After pulmonary surfactant administration, meropenem combined with vancomycin were given due to severe intrauterine infection and fluconazole was used to prevent fungal infection, the patient's condition improved after treatment. Two weeks after birth, bilateral paraventricular encephalomalacia was found by cranial ultrasound. Fever presented on the 33th day after birth, and the highest body temperature was 38.5℃, with decreased oxygen saturation and cyanosis. Sepsis workup was initiated and the results showed CRP 12.90mg/L, WBC 2.71x10^9/L, PLT 67x10^9/L, G test 505.8pg/ml. Piperacillin sodium and tazobactam sodium was given for the treatment of sepsis. Blood culture reported the growth of Candida glabrata. The infant was diagnosed as fungal septicemia. And lumbar puncture was performed, the result of CSF showed: WBC 1×10^6/L. Cl 109mmol/L, GLU 2.0mmol/L, protein 1937.8mg and cerebrospinal fluid culture showed aseptic growth. PICC catheter was removed and the culture of the tip of PICC reported the growth of Candida glabrata. After two weeks of treatment with amphotericin B, the infection index was normal, G test decreased (121.8pg/mL), blood culture turned negative. However, the level of CSF protein (2352mg/L) and white blood cells (12×10^6/L) was higher than those of the previous test, then he was diagnosed as Candida glabrata meningitis. Flucytosine was added for the treatment, and the parameters of CSF returned to normal after 1 week. No fungi was found in urine culture or stool culture, and no abnormalities were found in echocardiography, abdominal ultrasound and ophthalmoscope. Total treatment course for amphotericin B was 5 weeks and for flucytosine was 2 weeks. The cerebrospinal fluid returned to normal after treatment. The hepatic and renal function, serum electrolyte and blood routine were normal during treatment, and He was discharged home with good condition.

Discussion Periventricular leukomalacia was found in this case two weeks after birth, which is considered to be associated with severe intrauterine infection. Prematurity, low birth weight, mechanical ventilation, and the use of PICC and broad-spectrum antibiotics are high risk factors for fungal infection. Positive blood culture, and abnormal CSF, together with periventricular leukomalacia, the infant should be treated as soon as possible to prevent more serious neurologic impairment. However, the therapeutic effect of amphotericin B was not effective, CSF protein was even higher than before. After combined with flucytosine, CSF protein returned to normal.

And there were no adverse reactions such as hepatic and renal function injury and myelosuppression were found. It was reported that flucytosine has high concentration in CSF, low drug resistance and was relatively safe, but the side effects of drugs still need to be closely monitored.
Conclusion The findings of our case shows that combination of amphotericin-flucytosine therapy is effective and safe and can be used for refractory candida glabrata meningitis in preterm infants.

关键字 早产儿、真菌性脑膜炎、氟胞嘧啶联合两性霉素 B

分类：16. Neonatology 新生儿
1775

Changes of mortality and cause of death of preterm infants in a Neonatal Intensive Care Unit over the past 15 years in China

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Abstract：
Objective To investigate changes of mortality and causes of death of preterm infants in Neonatal Intensive Care Unit (NICU) in an university hospital from 2005 to 2020.
Methods The clinical data of preterm infants who died between January 2005 and December 2020 were collected. The mortality and causes of death of preterm infants within different epochs(EpochⅠ: January 2005 through December 2009, EpochⅡ: January 2010 through December 2014, EpochⅢ: January 2015 through December 2020) were analyzed.
Results 84 of 5498 hospitalized preterm infants (1.53%) died. The mortality fell significantly by times, it's 3.14% (41/1304) in Epoch Ⅰ, 1.18% (22/1860) in Epoch Ⅱ, and 0.90% (21/2334) in Epoch Ⅲ. 61 preterm infants (72.6%) died within 7 days after birth, 15(72.6%) died within 7-28 days after birth, and remaining 8 preterm infants (9.5%) died over 28 days after birth. Among the preterm infants who died, 96.3%(81/84) had definite abnormal perinatal factors, including premature rupture of membranes (24/84, 28.6%), abnormal amniotic fluid (24/84, 28.6%), Hypertensive Disorder Complicating Pregnancy(17/84, 20.2%) and Twin-Twin Transfusion Syndrome(TTTS, 15/84,17.9%). Among 72 cases of premature infant death at gestational age less than 34 weeks, 33 cases (45.8%) had not received prenatal glucocorticoid to promote fetal lung maturation, and 61 cases (84.7%) received pulmonary surfactant after birth. The three most common causes of death were pulmonary hemorrhage (26/84, 31.0%), congenital defect (11/84, 13.1%) and respiratory distress syndrome (RDS, 10/84, 11.9%). The percentage of premature infants died of RDS(0.4‰vs.6.9‰, P=0.00) and pulmonary hemorrhage (2.1‰vs.6.9‰, P=0.03) in Epoch Ⅲ decreased significantly compared with Epoch Ⅰ.
Conclusions Pulmonary hemorrhage, congenital defect and respiratory distress syndrome are the three most common causes of death in preterm infants in our hospital. Perinatal care is still needed to reduce or avoid the occurrence of preterm birth. For threatened preterm delivery with gestational age of <34 weeks, prenatal glucocorticoids should be given in time to promote fetal lung maturation.

关键字 新生儿、病死率、死亡原因
分类：16. Neonatology 新生儿

1777

Severe fetal anemia as the primary symptom of anti-CD36 antibody alloimmune thrombocytopenia: A rare case report and literature review

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Background Fetal/neonatal alloimmune thrombocytopenia (FNAIT) is a relatively rare hemorrhagic disease caused by incompatible platelet-associated antigens between the fetus and the mother. Human platelet antigen (HPA) incompatibility is the main cause of FNAIT, while FNAIT caused by anti-CD36 antibody is extremely rare. We report a rare case of anti-CD36 antibody alloimmune thrombocytopenia with severe fetal anemia as the primary symptom and review the literature of FNAIT caused by anti-CD36 antibody.

Objective To investigate the clinical characteristics and treatment of FNAIT caused by anti-CD36 antibody.

Case The patient was a full-term female infant who was delivered by cesarean section. Apgar scores were 10.Ultrasonography at 23 weeks of gestational age showed MCA-PSV 1.34 MoM, indicating mild anemia of the fetus. Umbilical puncture at the 24 weeks of gestational age showed HB 67g/L and PLT 322x10^9/L, and at 27+6 weeks of gestation, HB 83g/L and PLT 189x10^9/L, at 32 weeks of gestational age, HB 110g/L and PLT 131x10^9/L. Three intrauterine blood transfusions were performed and the ultrasonography showed no signs of fetal hydrops. Maternal peripheral blood exon gene sequencing: CD36 gene C. 329_330delAC, homozygous mutation, pathogenicity, associated with platelet glycoprotein IV deficiency (CD36). Irregular antibody (-). Platelet specific antibodies: GpIa/IIa positive, GpIV positive, HLA positive. The result of cord blood: no Platelet-associated antibodies and erythrocyte associated antibodies. Sanger sequencing : c.329_330delAC, heterozygosity. The mother induced labor 4 times due to "edema fetus" and 2 times due to "fetal death in utero" .No fetal chromosome examination was performed after the above 6 times of induced labor. There was no yellow staining, pallor, hemorrhagic spots, petechiae and ecchymosis after birth of the patient. Umbilical cord blood examination showed Hb 142g/L, PLT 96x10^9/L. And 5% IVIG was used for treatment. Reexamination 10 hours after birth showed Hb 128g/L, PLT 134x10^9/L, and 2 days after birth showed Hb 137g/L, PLT 194x10^9/L. Ultrasonography of brain showed no abnormalities. Platelets and hemoglobin were normal after discharge, and the growth and development of the child was normal.

Results A total of 11 cases of FNAIT induced by anti-CD36 antibody were reviewed and summarized by literature review. The clinical manifestations of FNAIT were different: four cases presented with hemorrhagic spots, petechiae, ecchymosis and hematoma after birth, and 4 cases presented with fetal edema and anemia as the primary symptoms, accompanied by intrauterine or postnatal thrombocytopenia. The remaining 3 cases showed only postnatal platelet count reduction without bleeding. The case reported in this report started with severe fetal anemia. Due to timely intrauterine red blood cell transfusion, no obvious fetal edema was observed, and thrombocytopenia occurred after birth. At present, there is no unified standard for the treatment of FNAIT induced by anti-CD36 antibody, which mainly consists of prenatal and postnatal red blood cell and platelet transfusion, glucocorticoid application and IVIG. Of all the cases reviewed, there were only 2 cases with only postnatal thrombocytopenia without special treatment, and platelets spontaneously returned to normal.

Conclusion anti-CD36 antibody can cause FNAIT and its clinical manifestation has different characteristics. For fetuses with intrauterine anemia, fetal edema,

intrauterine or postnatal thrombocytopenia, not only should we consider testing for blood incompatible-associated antibodies to exclude isoimmune hemolytic disease, but also do testing of platelet-associated antibodies. In addition, whole exon gene sequencing can be performed to assist diagnosis if necessary. Hemoglobin and platelet status should be monitored regularly, and timely intervention should be performed when indicated to avoid adverse outcome.

关键字 病例报道、新生儿血小板减少症、水肿、贫血、CD36

Epigenetics Physical Activity

表观遗传学

分类：10. Epigenetics Physical Activity 表观遗传学 运动
823

The effect of physical activity on the distribution of subcutaneous fat in 7-12 aged children

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Backgrounds: Fat is stored in the body in different compartments. The two main compartments are subcutaneous (under the skin) and visceral (around the internal organs). Subcutaneous fat is the main sign of overweight and obesity. It can be affected by genes, energy intake, physical activity, lifestyle and diseases. Previous studies have focused on the age-related changes and gender differences of subcutaneous fat of school-aged children. However, it remains unclear about the distribution of local subcutaneous fat of children aged 7-12 and the effect of physical activity on local subcutaneous fat.

Methods: 360 school-age children (aged 7-12 years) participated in the study. They are divided into six age groups. Each age group has half boys and half girls. The local subcutaneous fat distribution index of the upper arm, abdomen, upper and lower legs were collected by a fat detector based on the principle of bioelectrical impedance. A physical activity questionnaire for school-aged children was also collected. Two-way ANOVA was used to investigate the effects of age and gender on the subcutaneous fat distribution index; one-way ANOVA was used to investigate the effect of frequency and intensity of physical activity on the subcutaneous fat distribution index.

Results: The study found that (1) age and gender had a significant effect on the subcutaneous fat distribution of the thigh of school-age children aged 7-12. (2) According to the post-doc test, the fat distribution index of the thigh of girls is larger, reflecting that the subcutaneous fat of girls has the characteristics of "centralized body fat distribution". (3) The distribution index of subcutaneous fat of abdomen of school-age children was significantly affected by age. (4) The total subcutaneous fat distribution index of school-age children is positively correlated with BMI ($r=0.616$, $P<0.01$). (5) The intensity of physical activity had a significant effect on the total subcutaneous fat distribution index in school-aged children instead of the frequency of physical activity.

Conclusions: These results show that the distribution of subcutaneous fat in school-age children aged 7-12 has age and gender characteristics, and the intensity of physical activity at school has a positive effect on reducing subcutaneous fat.

关键字 physical activity, subcutaneous fat, school-aged children

分类：10. Epigenetics Physical Activity 表观遗传学 运动
1028

High folate corn callback one carbon metabolism more effectively than folic acid in folate-deficient mice

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Objective To figure out the improvement effect of natural folates on folate deficiency, and compare FA metabolisms and methylation regulations of nature high folate corn with synthetic folic acid in folate-deficient mice.
Methods A high-folate inbred line was used to figure out the effects of natural folates in plants on folate deficiency. Respectively, the normal-folate variety was chosen due to its high yield, stable yield, high quality, multi resistance and wide adaptability in China during the last 20 years. Except these two lines of corn, synthetic folic acid with different levels were also designed to add into diet to compare supplementary effects of nature high folate corn with synthetic folic acid in folate-deficient mice. C57BL/6J mice were fed folate-deficient for 4 weeks to build a folate-deficient status, and then kinds of folate-supplemented diets were supplemented for mice until euthanized on E18.5. FA metabolisms and methylation levels were tested to compare the effect of FA supplementary with different types of FA.
Results A high-folate inbred line has efficient impact on folate deficiency. After 4 weeks with high folate corn intake, the levels of FA metabolisms and methylation modifications recalled back, however the supplementary effort changed drastically according to the FA supplement form, the highest-efficiency of FA utilization exist in high folate corn diet group. Both global methylation level and LINE-1 methylation level were call backed with FA supplementary in FA-deficient mice, and our data implying a more effectively methylation callback of high folate corn. Furthermore, restricted retrotransposon activity regulated by hypermethylation of LINE-1 and orderly pattern of phospholipid/lipid metabolism in high folate corn group ensure a health status for development.
Conclusions Our analysis suggested that biofortification folate corn could be taken as a better cost-effective, sustainable, and easily accessible fortification food to meet folate deficiency.

关键字 High folate corn; folate; methylation; retrotransposon; phospholipid/lipid metabolism

Category: 10. Epigenetics Physical Activity 表观遗传学 运动
1046

The epigenetic mechanisms of Chinese herbal antagonizes Bisphenol A on Kiss1 gene expression

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Abstract Content Backgroup:
A (BPA), an environmental endocrine disruptor, is often associated with precocious puberty. Chinese Herb Medicine for Nourishing Yin and Purging Fire (NYPF) has been effective in delaying the process of puberty. However, the underline mechanism is unknown. Epigenetic plays an important role in environmental and nutritional factors modulating puberty. We intend to investigate the epigenetic impact of Bisphenol A and NYPF herbs on the Kiss1 gene, an vital gene driven puberty onset, in hypothalamic neuron cells.

Methods GT1-7 hypothalamic neuron cell line was used in this study. Series of concentrations (500ng-10mg/L) of BPA were prepared, as well as serum samples mediated by NYPF herbs or saline. The GT1-7 cells were cultured with either BPA or in combination with NYPF herbs for 24 hours. Quantification of Kiss1 gene expressions were performed by Realtime-PCR and Weston-blot metheods. In addition, Bisulphite Sequencing (BSP) method were used to detect the CpG methylation status of Kiss1 gene promoter. And Chromatin histone modification was examined by means of chromatin immunoprecipitation assay combined real-time PCR (Chip-qpcr) at the Kiss1 gene promoter.

Results (1) The expression of Kiss1 gene: The 10 mg/L BPA group exhibited an increase in both mRNA and protein levels of Kiss1, as well as GnRH1. On the contrary, TCM treated group showed a significant decline in the expressions of this two genes. (2) Epigenetics modification at Kiss1 gene promoter: Lower methylation status was detected in BPA group than control (61.25% Vs. 76.56%), accompanied by increased level of mixed-lineage leukemia 1(MLL1: 1.05%±0.15 Vs. 0.27%±0.01) and Tri-Methyl-Histone 3 at lysine 4(H3K4me3: 0.77%±0.51 Vs. 0.02%±0.04) recruitment at the promoter with BPA administration. After TCM for NYPF administration, the methylation level of Kiss1 gene promoter increased to 83.75%, and MLL1/H3K4me3 quantity presented decline trends (MLL1: 0.14%±0.02 Vs. 0.97%±0.09 ; H3K4me3: 0.01%±0.00 Vs. 0.57%±0.30).

Conclusion These results indicated that BPA can induce high expression of Kiss1 gene through alteration of CpG methylation and chromatin conformation at Kiss1 promoter in GT1-7 cells. On the contrary, TCM can reverse the effect of BPA on Kiss1 gene expression by epigenetic regulation of Kiss1 gene promoter.

Key words Bisphenol A, Chinese herb, Nourishing Yin Purging Fire, Kiss1, epigenetic
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分类：10. Epigenetics Physical Activity 表观遗传学 运动
1048

MiR370 at the imprinted Dlk1-Dio3 domain activated by folate deficiency interacts with DNMT3a during embryonic development

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BACKGROUND: Dlk1-dio3 is an imprinted domain, the largest microRNAs cluster found in the human genome.We focus on the domain to explore the effect of low folate nutrition on imprinting modification in early development and then regulate the expression of downstream ncRNA and its target genes, thus revealing the possible mechanism of folate deficiency affecting multiple developmental pathways.
METHODS：Ⅰ.Neural tube defects and normal aborted embryos were selected to compare the folate concentration and the methylation modification of DMRs in neural tissues.Ⅱ. Cell models:(1) mESCs cultured in medium with different folate concentration: detecting the methylation rate of DLK1-DIO3 and the expression of downstream ncRNA by expression profiling chip,as well as the DNMT3A-enriched fragments by Chromatin Immunoprecipitation. (2) 293T cell: Luciferase assay was used to confirm the target regulation of miR370 on DNMT3a. (3) SK-N-SH cells: Changes in methylation in DMRs and cell function were detected after miR370 was overexpressed. Ⅲ. Folate-deficienct mouse model: Female mice were fed an FA-free diet for 4 wk. Fetal mice were obtained from pregnant mice at a gestational age of 13.5 days. The brain development of fetal mice was observed by immunohistochemistry, and the expression of miR370 and DNMT3A in the brain and methylation rate of DMRs were detected. IV. Different doses of miR370 were overexpressed in zebrafish embryos to explore the influence of miR370 on embryo development.
RESULTS：Ⅰ.The concentration of folate in the NTDs group was lower than that in the Control group ($P<0.01$); IG-DMR and MEG3-DMR imprinting modification were reduced ($P<0.05$) in NTDs group.Ⅱ. (1) The methylation rate of IG-DMR, GTL2-DMR, and DLK-DMR were decreased in mESCs cultured in low-folate-medium ($P <0.05$); Downstream Rian-derived miR370 is negatively correlated with the methylation rate of IG-DMR, GTL2-DMR and DLK-DMR. (2) Luciferase assay confirmed that miR370 could inhibit the expression of dnmt3a. After transfection with miR370 mimic in 293 T cells, the expression of dnmt3a decreased by 34%. (3) After miR370 was overexpressed in SK-N-SH cells, the expression of dnmt3a was inhibited by nearly 80%, and the migration ability of SK-N-SH cells was weakened. (4) Chromatin Immunoprecipitation of DNMT3A showed that the signal of DNMT3A-enriched fragments was significantly weakened with low folate intervention, and differential genes were enriched in developmental and metabolic pathways.Ⅲ、In folate-deficient mouse models, neural development was significantly delayed. Compared with the control group, fetal mice at 13.5 days, telencephalon and midbrain cortical thickness and brain tissue area were decreased in the folate-deficient group($P<0.01$). Further studies found that in the neural tissues of folate-deficient mice, imprinting methylation of IG-DMR, GTL2-DMR, and DLK-DMR was reduced. Among them，GTL2-DMR and DLK-DMR had statistical differences. Also, miR-370 expression was activated and the expression of Dnmt3a was suppressed($P<0.05$).Ⅳ、A zebrafish model overexpressing miR370 suggested that the incidence and severity of NTDs in the miR370-200nm subgroup were significantly higher than those in group miR370-100nm and miR370-NC.
CONCLUSION:Perinatal low folate nutrition can reduce the imprinted methylation of the imprinted Dlk1-Dio3 Cluster, and interfere with its cis-regulatory on downstream non-coding region-Meg8/Rian, which in turn activates miR-370 expression, while the

expression and binding ability of DNMT3a within and outside the imprinted region were inhibited, ultimately impairing early embryo development. Our study confirmed that folate deficiency could lead to imprinting disorders of the Dlk1-Dio3 imprinting gene cluster at the human, animal, and cellular levels.However, the mechanism of how dnmt3a, as the target gene of miR370, affects the imprinting network and its downstream signaling pathways under folate intervention needs to be further explored.

关键字 Imprinted genes, folic acid, DLK1-Dio3, embryonic development

分类：10. Epigenetics Physical Activity 表观遗传学 运动

1125

High H3K79hcy regulates the abnormal modification of H3K4me3: Implications in the occurrence of NTDs induced by high Hcy

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Background: Maternal high Homocysteine (Hcy) is a risk factor for fetal neural tube defects (NTDs). Our previous studies showed that in the hyper-homocysteine induced NTDs chicken embryo and neural stem cell modes, the histone H3K79hcy modification increased abnormally, accompanied by the down-regulation of H3K4me3 modification, but the mechanism is not clear. Aims: The purpose of this study is to determine whether there is crosstalk between histone H3K79hcy and H3K4me3 modification under the induction of high Hcy and its downstream effects. Methods: In the high Hcy induced neural stem cell model and NTDs chicken embryo model, we used chromatin immunocoprecipitation (ChIP) technology to detect whether H3K79hcy regulated the expression of H3K4me3 related modifying enzymes such as Menin，Kmt2a、Wdr82. Western was used to detect the protein expression level of H3K4me3 modifying enzymes. RNA interference knockdown technology or overexpression technology was used to detect the regulatory mechanism of Menin, the key modifying enzyme of H3K4me3 on DNA damage repair. Results: Under the induction of high Hcy, H3K79hcy regulates the expression of histone H3K4me3 modifying enzyme gene, among which Menin expression is down-regulated most significantly. The knockdown and overexpression experiments of Menin further confirmed that it is the key regulatory molecule causing the down regulation of H3K4me3 under high Hcy. This abnormal regulation further leads to the disorder of DNA damage repair mechanism, especially the impact on DNA transcription repair pathway genes. Conclusions: The high level of H3K79hcy modification caused by high Hcy may further cause the abnormality of H3K4me3 modification, further impact DNA transcription repair pathway and thus participate in the occurrence of NTDs.

关键字 H3K79hcy ; H3K4me3 ; Menin; DNA transcription repair pathway; Neural tube defects

分类：10. Epigenetics Physical Activity 表观遗传学 运动

1153

Aberrant PEG10 methylation associated with folate deficiency is involved in human spina bifida

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Background: Paternally expressed gene 10 (PEG10) is believed to be a key imprinted gene involved in placenta formation. However, its role in human folate-related spina bifida remains unclear.
Methods: The methylation status of the differentially methylated region (DMR) in the PEG10/sarcoglycan epsilon (SGCE) imprinted cluster was compared in spina bifida patients and control samples. Moreover, the influence of ectopic PEG10 expression on apoptosis was assessed to explore the underlying mechanisms related to folate deficiency-induced aberrant PEG10 imprinting in spina bifida.
Results: The case group exhibited a significant increase in the methylation level of the DMR and a marked reduction in the mRNA and protein expression of PEG10 compared with the control group. A prominent negative correlation was found between the folate level in brain tissue and DMR methylation status ($r=-0.62$, $P=0.001$). A cell model treated with a demethylating agent showed significant elevation in the transcription levels of the PEG10 gene, as well as other imprinted genes in the same cluster. In addition, the inhibition of PEG10 was found to be accompanied by aberrant activation of apoptosis in spina bifida.
Conclusion: Our findings suggest that disturbed imprinted modification of PEG10 due to folate deficiency is involved in spina bifida through aberrant activation of apoptosis.

关键字 Folate deficiency, methylation modification, imprinted gene, spina bifida

分类：10. Epigenetics Physical Activity 表观遗传学 运动

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Elevated homocystein inhibits cell proliferation through histone homocysteinylation during neural development and subsequent neural tube defects

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Background: Maternal nutritional factors hyperhomocysteinemia during pregnancy is associated with increased risk of Neural tube defects (NTDs) in the offspring, while its mechanism remains elusive.
Methods: First the nutritional factors homocystein metabolite, homocysteine thyolactone (HTL) was used to induce NTDs model in chicken embryo. The neural groove of incubated white leghorms eggs were injected with 0.5mM HTL to induce NTDs model. Then the cell proliferation level were studied by Immunohistochemistry and immunofluorescence in HTL induced chicken NTDs and HTL treated NE4C cells (Mouse neural stem cells). Further, the cell proliferation pathway related to NTDs were studied by RNA-seq in NE4C cells. At last, whether cell proliferation pathway genes were regulated by histone homocysteinylation were studied by ChIP-seq .
Results: We got the HTL-induced chicken NTDs successfully. We found that cell proliferation decreased by PCNA (Proliferating Cell Nuclear Antigen) and SABC (strept avidin-biotin complex) test in HTL-treated chick NTDs. Further, we confirmed that cell proliferation decreased by Edu (5-ethynyl-2’-deoxyuridine) test in HTL treated NE4C cells. Then we found that the protein level of cell proliferation related MAPK pathway genes Fgf13 and Kras decreased in HTL induced chicken NTDs and HTLtreated NE4C cells. At last we found that MAPK pathway genes were regulated by histone homocysteinylation by ChIP-seq and RNA-seq.
Conclusion: Our results suggest that nutritional imbalance and metabolic disorder such as higher levels of homocystein contribute to the onset of NTDs through histone homocysteinylation, leading to abnormal expressions of proliferation genes during the early stage of neural development and subsequent neural tube defects.

关键字 neural tube defects, histone homocysteinylation, cell proliferation, homocysteine, chicken NTDs model

分类：10. Epigenetics Physical Activity 表观遗传学 运动

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Induced histone H2BK120 monoubiquitination lead to abnormal genes expression involved in neural tube defects

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Objective To investigate the mechanism about the regulation of the histone H2BK120 monoubiquitination on neural tube development genes, which would provide new epigenetic mechanisms of the NTDs induced by environmental factors from the perspective.
Methods In retinoic acid (RA)-induced C57BL / 6J mouse neural tube malformation, the change of neural tube development genes Pax6、Nestin was detected by Q - PCR, and the changes of histone H2BK120ub1 were detected by Western Blot and immunohistochemical. Chromatic Immunoprecipitation (ChIP)-seq and Q - PCR was used to detect the changes of histone ubiquitination and the binding with Pax6、Nestin genes. Elisa detected levels of retinoid and vitamin A. In F9 (Mouse embryonal carcinoma) cells, the Pax6、Nestin genes was detected by Q - PCR after knockdown USP22 or / and RA. In the human anencephaly NTDs clinical samples, the changes of the selected PAX6、NESTIN genes were detected by the fluorescent bar code labeling single molecule detection technique (Nanostring nCounter), and the Western Blot was used to detect the changes of H2BK120ub1.
Results Here, we show that upregulation of neural tube development genes Pax6、Nestin genes was observed along with higher levels of H2BK120ub1 both mouse and human anencephaly NTDs cases. Notably, the expression of PAX6、NESTIN genes was positively correlated with H2BK120ub1 levels in human anencephaly NTD cases. The deubiquitylase USP22 is required for the activation of RA- inducible Pax6、Nestin expression in F9 cells. In addition, RA treatment led to induce H2BK120ub1 due to decrease in deubiquitylase USP22, further affecting Pax6、Nestin gene regulation.
Conclusions Our results indicate that abnormal Pax6、Nestin gene expression induced by aberrant H2BK120ub1 levels may be a risk factor for NTDs, and highlight the need for further analysis of genome-wide epigenetic modifications in NTDs.

关键字 [Key words] Neural tube defects (NTDs); Histone ubiquitination; RA; neural tube development genes

分类：10. Epigenetics Physical Activity 表观遗传学 运动

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Effect of COVID-19 pandemic on physical activity, sedentary behaviour and sleep and associations with adiposity among pre-school children: A cohort study in urban Beijing, China

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Abstract
Background: The COVID-19 pandemic has placed unprecedented restrictions on children's ability to participate in healthy levels of movement behaviours. The aim of this study was to investigate how COVID-19 movement restrictions affected physical activity, sedentary behaviour and sleep patterns and their associations with adiposity in a sample of pre-school children, and how this has changed compared to pre-COVID-19.
Methods: Participants were 196 kindergarten children aged 4.3-6.3 years, recruited from one kindergarten in an urban area of Beijing. Participants had completed a survey pre-COVID in September to October 2019 and were asked to complete the survey again during the pandemic in May to June 2020. Physical activity, sedentary screen time and sleep duration were assessed via parent questionnaire on behalf of the participating child. The children's overweight or obesity status, follow-up anthropometric data was collected according to standard procedures by kindergarten teachers. Frequency analyses were performed to examine the proportion of children meeting the WHO guidelines individually for each behaviour and in combination. Logistics regression analyses were conducted to examine the associations between physical activity changes and COVID-19 exposures, the associations between adiposity and physical activity changes.
Results: 196 parents completed the survey at both time points. The proportion of children who met the physical activity (TPA) guideline (≥180min daily physical activity, including ≥60min daily moderate to vigorous-intensity physical activity (MVPA)), sedentary screen time (≤60min/day), sleep guidelines (10-13h/day) and all four guidelines were 35.70%, 85.70%, 90.81% and 29.08% respectively pre-COVID-19, and were 22.45%, 47.45%, 86.73% and 6.63% respectively during the COVID-19. There were significant differences in healthy movement behaviours, and associated factors (bedtime, wake-time, time spent outdoors and sleep quality) among preschool children before and during the COVID-19 pandemic. The percentage of overweight or obese children had increased from 3% to 19%, and children whose parents reported an increase in sedentary screen time during the COVID-19 were at higher risk for overweight and obesity (odds ratio=0.99, 95% CI: 0.980 - 0.999).
Conclusions: The study confirms the proportion of children who met the physical activity guidelines was lower, and sedentary screen time was higher, during the COVID-19 compared to pre-COVID-19. Changes in sedentary screen time in relation to COVID-19 may become permanently entrenched, leading to increased risk of obesity in children. Campaigns aiming at further interventions for limiting screen time and healthy movement behaviours in young children are important prevention strategies.
关键字 24-hour movement behaviours; sedentary behaviour; sleep; pre-school; COVID-19 pandemic
分类：10. Epigenetics Physical Activity 表观遗传学 运动

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Reliability and Validity of Physical Activity Questionnaire for preschooler (P-PAQ)

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Background

Physical activity (PA) in early years is related to their growth,fundamental motor skill,mental,cognitive social ability and emotional development.Research shows that lack of exercise is one of the important factors causing adiposity in preschool children.So it's necessary to develop physical activity monitoring and guidance for children,especially preschool children.At present, Accelerometers are reliable and valid objective instruments for measuring PA,but It is expensive and time-consuming.Compared with it,questionnaires is practical,easy to implement in population surveillance studies,and provide important contextual information about PA and sedentary behavior (SB).CDC reported the physical activity questionnaire for children aged 10-17 years old,However,there is not yet appropriate physical activity questionnaire for preschoolers at the age of 3-6 years old in China.So the aim is to develop Physical Activity Questionnaire for Preschooler (P-PAQ) and examine its reliability and validity, providing a reliable and effective measuring tool for assessing Chinese preschooler’s physical activity.

Method

Physical Activity Questionnaire of Preschooler

The P-PAQ was developed in five strategies:1)review of the literature;2)examination of existing, validated, physical activity questionnaires;3)designing the questionnaire format,content and flow;4)consulting Chinese physical activity experts and conducting focus groups with parents and preschool staff and then revising the questionnaire and 5)pilot testing.P-PAQ is a 7-day recall physical activity questionnaire designed to measure physical activity and sedentary behavior in child's home environment.It is mainly composed of physical activity outside the kindergarten on weekdays and weekends.Assessment of the child's physical activity included a list of activities typical in preschool children with a response of 'YES'or 'NO',and if 'YES',the child's time spent in the activity needs to be answered.P-PAQ is completed by the main caregivers who are familiar with children's daily activities and takes 20 ~ 30 minutes.

Accelerometer Data Management

Physical activity was assessed using ActiGraph GT9X+ accelerometer as criterion method on the basis of its established reliability and accuracy.For this study, the accelerometer was set to record data at a sampling rate of 30 Hz and re-integrated into 15-s epochs for analyses.The sleeping time of each individual was marked as non-wear time. The minimum wear-time for inclusion in the analysis was at least 5h per day off campus on weekdays and 8h per day on weekends for at least 3 days (including at least 2 weekdays and 1 weekend days).The intensity of physical activity was defined using the cut points derived by Pate et al (2006).

Participant

Recruitment was conducted in three kindergartens in Beijing,Shenyang and Xi'an,from November to December,2020 utilizing a convenience cluster sampling

method among children aged 3-6 years old.The P-PAQ was administered for two times in 225 children to examine reliability by using intraclass correlation coefficients.To assess validity, 229 participants wore accelerometers for a 7-day monitoring period and then completed P-PAQ measures Data.Using Spearman’s correlation coefficient and the Bland-Altman plots to assess the validity.
Result
The reliability coefficient of the P-PAQ ranged from 0.64 to 0.84,referring to good reliability.Spearman's correlation coefficient for validity of time spent on MVPA on weekdays and weekends were 0.153 and 0.151,respectively (P<0.05).The correlation for validity of girls on weekends was 0.237(P<0.05).Mean min/day of PA estimated from P-PAQ were significantly lower than those obtained by accelerometry.96% of the data were in the confidence interval (95% CI), indicating that the data have a good consistency level.
Conclusion
P-PAQ showed good reliability and Validity and can be used to investigate physical activity time on different intensity among preschoolers.

关键字 Preschooler; Physical activity; Off campus; reliability; validity

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Protective effect of Magnoflorine with Hyaluronic Acid Gel on Cartilage Degeneration in a rat model of ACLT induced Osteoarthritis

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Objective: To investigate efficacy of Chinese medicine magnoflorine combined with hyaluronic acid (HA)-gel in attenuating cartilage degeneration in traumatic osteoarthritis (OA).

Methods: The viability, cell proliferation and migration rate of chondrogenic cells under magnoflorine treatment was measured. Chondrogenesis was stained by Alcian Blue. The chondrogenic related gene expressions were confirmed by qPCR. The surgery of anterior cruciate ligament transection (ACLT) was made at right hind limbs of 8-week-old female rats and resulted in a traumatic OA. Rats (n=5/group) were treated once intra-articular injection of 50μl HA-gel, 50μl HA-gel+100μg/kg magnoflorine, 50μl of saline+100μg/kg magnoflorine, null (ACLT group) respectively except sham group. Limbs were harvested for μCT scan and histopathological staining 3-month post-surgery. Inflammatory cytokines from synovial fluid were detected using Immunology Multiplex Assay kit.

Results: 50μg/ml magnoflorine treatment significantly increased the viability, S-phase, migration rate and chondrogenesis of chondrogenic cells. There was a significant downregulation of MAPK and NF-κB, and an upregulation of chondrogenesis signaling pathway related genes in 50μg/ml magnoflorine treatment. There also a significantly down-regulated inflammatory cytokines and upregulated anti-inflammatory cytokine IL-10 in HA+Magnoflorine group. In vivo, HA-gel+magnoflorine treatment significantly altered subchondral bone structure changes included increase in BV/TV, Tb.Th, and decrease in Tb.Pf, Po(tot), Conn.Dn and Tb.Sp, which implied a protective effect on maintaining the stabilization of trabecular bone microstructure. Treatment also resulted in the decreased modified Mankin's scores, higher volume ratio of hyaline cartilage (HC)/calcified cartilage (CC) and HC/Sum (total volume of cartilage), compared to ACLT and HA-gel group. Furthermore, both the volume ratio of HC/Sum and HC/CC were negatively correlated with the modified Mankin's scores. Finally, histological results showed the elevated cartilage matrix, chondrogenic signaling and chondrogenic cells in HA-gel+magnoflorine treatment.

Conclusion: Our study elucidated the potential benefits of HA-gel+magnoflorine in revealing a protective effect on attenuating cartilage degradation and maintaining subchondral bone stabilization in ACLT induced OA.

关键字 Osteoarthritis，Hyaluronic acid，Magnoflorine，Cartilage，Subchondral bone

分类：10. Epigenetics Physical Activity 表观遗传学 运动

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Lingzhi and San-Miao-San with hyaluronic acid gel mitigate cartilage degeneration in anterior cruciate ligament transection induced osteoarthritis

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Objective: To investigate the mitigate efficacy of Chinese medicine Lingzhi (LZ) and San-Miao-San (SMS) combined with hyaluronic acid (HA)-gel in attenuating cartilage degeneration in traumatic osteoarthritis (OA).

Methods: The standardized surgery of anterior cruciate ligament transection (ACLT) was made from the medial compartment of right hind limbs of 8-week-old female SD rats and resulted in a traumatic OA. Rats (n=5/group) were treated once intra-articular injection of 50 μl HA-gel, 50 μl HA-gel+50 μg LZ-SMS, 50 μl of saline+50 μg LZ-SMS and null (ACLT group) respectively, except sham group. Limbs were harvested for μCT scan and histopathological staining 3-month post-treatment. Inflammatory cytokines from plasma and synovial fluid were detected using Immunology Multiplex Assay kit. The putative targets of active compounds in LZ-SMS and known therapeutic targets for OA were combined to construct protein-protein interaction network. Gene Ontology and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis was adopted to predict the potential targets and signaling pathway of LZ-SMS in OA through the tool of DAVID Bioinformatics.

Results: In vivo, HA-gel + LZ-SMS treatment resulted in a higher volume ratio of hyaline cartilage (HC)/calcified cartilage (CC) and HC/Sum (total volume of cartilage), compared to ACLT and HA-gel groups. In addition, histological results showed the elevated cartilage matrix, chondrogenic and osteoblastic signals in HA-gel + LZ-SMS treatment. Treatment also significantly altered subchondral bone (SCB) structure including an increase in BV/TV, Tb.Th, BMD, Conn.Dn, Tb.N, and DA, as well as a significant decrease in Tb.Sp and Po(tot), which implied a protective effect on maintaining the stabilization of tibial SCB microstructure. Furthermore, there was also a down-regulated inflammatory cytokines and upregulated anti-inflammatory cytokine IL-10 in HA+LZ-SMS group. Finally, 64 shared targets from 37 active compounds in LZ-SMS related to the core genes for the development of OA. LZ-SMS has a putative role in regulating inflammatory circumstance through influencing the MAPK signaling pathway.

Conclusion: Our study elucidated a protective effect of HA-gel + LZ-SMS in mitigating cartilage degradation and putative interaction with targets and signaling pathway for the development of traumatic OA.

关键字 LZ-SMS; osteoarthritis; articular cartilage; subchondral trabecular bone; hyaluronic acid gel

分类：10. Epigenetics Physical Activity 表观遗传学 运动

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Two novel mutations in TCIRG1 induced infantile malignant osteopetrosis: a case report

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Background: Infantile malignant osteopetrosis (IMO) is a rare autosomal recessive disease characterized by a higher bone density in bone marrow caused by the dysfunction of bone resorption. Clinically, IMO can be diagnosed with medical examination, bone mineral density test and whole genome sequencing.
Case presentation: We present the case of a 4-month-old male infant with abnormal skull development, hypocalcemia and premature closure of the cranial sutures. Due to the hyper bone density showed by his radiographic examination, which are characteristic patterns of IMO, we speculated that he might be an IMO patient. In order to confirm this diagnosis, a high-precision whole exome sequencing of the infant and his parents was performed. The analysis of high-precision whole exome sequencing results lead to the identification of two novel heterozygous mutations c.504-1G > C (a splicing site mutation) and c.1371delC (p.G458Afs*70, a frameshift mutation) in gene TCIRG1 derived from his parents. Therefore, we propose that there is a close association between these two mutations and the onset of IMO.
Conclusions: To date, these two novel mutations in gene TCIRG1 have not been reported in the reference gene database of Chinese population. These variants have likewise not been reported outside of China in the Genome Aggregation Database (gnomAD). Our case suggests that the use of whole exome sequencing to detect these two mutations will improve the identification and early diagnosis of IMO, and more specifically, the identification of homozygous individuals with TCIRG1 gene mutation. We propose that these mutations in gene TCIRG1 could be a novel therapeutic target for the IMO in the future.

关键字 Infantile malignant osteopetrosis, TCIRG1, Mutation, Autosomal recessive osteopetrosis

分类：10. Epigenetics Physical Activity 表观遗传学 运动
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Folate deficiency induced Histone H3 lysine 79 dimethylation lead to downregulation of genes involved in neural tube defects

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Objective: To investigate the mechanism about the regulation of the histone H3 lysine 79 dimethylation (H3K79me2) on Neural tube defects (NTDs), which would provide new epigenetic mechanisms of the NTDs induced by folate deficiency.
Methods: In C57BL/6J mouse neural tube malformation induced by low folic acid diet and methotrexate (MTX), the changes of disruptor of telomeric silencing 1-like (DOT1L) gene and sonic hedgehog (Shh)-related genes SHH, SUFU were detected by RT-qPCR, and the changes of DOT1L, H3K79me2 were detected by Western Blotting. In mouse embryonic stem cells (mESCs), the SHH and SUFU genes were detected by RT-qPCR and ChIP-qPCR after folate deficiency, or/and DOT1L knockdown, MTX reduction. And the changes of DOT1L, H3K79me2 were detected by western blotting and Immunofluorescence. In addition, We analyzed equal number of reads with ChIP-seq and statistical enrichment levels of H3K79me2 and target genes in mESCs. We also investigated the extent of H3K79me2 by ChIP enrichment on SHH and SUFU genes in mESCs after MTX treatment. In brain and spinal tissues of human NTD fetuses, we detected the levels of DOT1L, H3K79me2 by western blotting, and the expressions of SHH, SUFU genes by Nanostring.
Results: We demonstrated that an decrease in H3K79me2 downregulation of the SHH, SUFU genes in mESC under folate defciency. We also found that DOT1L was responsible for MTX reduction in H3K79me2 and subsequently affecting expression of SHH and SUFU genes. Moreover, folic acid supplementation restored H3K79me2 binding to neural tube closure-related genes. We further confirmed that SHH and SUFU genes were downregulated in mouse brain and human NTDs. Moreover, lower levels of H3K79me2 were found in maternal serum under folate defiency induced mouse NTDs. Statistical analysis showed H3K79me2 levels decreased correlation down-regulated expression of the neural tube closure-related genes.
Conclusions: This study indicates that folate deficiency contributes to NTDs by altering H3K79me2 and had influcence on the expression of SHH, SUFU genes. Disrupted H3K79me2 levels may responds to folate deficiency and promote NTDs. We conclude that folate deficiency contributes to neural tube defects by changing the level of H3K79me2 and genes, which are related with neural tube closure.

关键字 Histone methylation, Neural tube defects (NTDs), Methotrexate (MTX), Disruptor of telomeric silencing 1-like (DOT1L), Sonic hedgehog (Shh)-related genes

分类：10. Epigenetics Physical Activity 表观遗传学 运动
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Downregulation of cholesterol biosynthesis via SIRT2 potentially mediates the development of folate deficiency-induced neural tube defects

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Objective: Sirtuins can promote deacetylation of a wide range of substrates in diverse areas to regulate many cellular processes. Herein, we investigate the mechanism of SIRT2 as a critical protein regulates the process of the cholesterol biosynthesis in folate deficiency induced neural tube defects (NTDs).
Methods: Genome wide profiles of mRNA expression were completed in 24 pairs of human NTDs brain tissue samples, cholesterol biosynthesis related genes were found and their protein and mRNA levels were verified by western blot and quantitative real-time PCR. Cholesterol biosynthesis related proteins were analyzed by Immunohistochemstry (IHC) to show their nucleus localization. In mouse embryonic stem cells (mESCs), the *Sirt2*, *Srepb2* and candidate cholesterol synthesis pathway genes was detected by RT-qPCR. In C57BL/6J mouse neural tube malformation induced by low folic acid diet and methotrexate (MTX), the changes of *Sirt2*, *Srepb2* and candidate cholesterol synthesis pathway genes were detected by RT-qPCR, and the changes of SIRT2 and SREPB2 were detected by Western Blotting. In brain and spinal tissues of human NTD fetuses, we detect the SIRT2 and SREBP2 by western blotting, and the 14 candidate cholesterol synthesis pathway genes by Nanostring.
Results: Here, we found that downregulation of genes related to cholesterol biosynthesis, *HMGCS1*, *HMGCR MVD* , *IDI1*, *FDFT1*, *SQLE* , *CYP51A1*, *DHCR7*, *DHCR24*, *SC4MOL*, *TM7SF2*, *MVK*, *NSDHL*, *EBP*, *FDPS*, *LSS* were observed along with SIRT2 suppression in human NTDs cases. Inhibition of SIRT2 led to decrease in cholesterol biosynthesis. Western blot and RT-qPCR confirmed that their protein and mRNA levels are consistent with microarray analysis. SIRT2, MVD and IDI1 decreased significantly in the NTDs fetuses. SIRT2 and SREBP2 showed significant increase in nucleus localization in NTDs in response to the insufficiency of endogenous cholesterol. Folate depletion decreased the levels of SIRT2 and cholesterol biosynthesis in our cellular models. We also found that downregulation of Sirt2, Srepb2 and candidate cholesterol synthesis pathway genes were observed in both brain tissue of mouse and human NTD cases, and low levels of SIRT2 and SREBP2 were found in the corresponding NTDs samples with their maternal serum folate under low levels.
Conclusions: Our results indicated that folate as genetic environmental factor intervened neural tube closure through downregulation in cholesterol synthesis by inhibition of SIRT2 and SREBP2. Disruption in folate metabolism could significantly interrupt cholesterol biosynthesis to lead to NTDs.

关键字 Neural tube defects; Folate deficiency; Cholesterol; Sirtuin2; Srepb2

分类：10. Epigenetics Physical Activity 表观遗传学 运动
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Folate deficiency reduced TET2 expression to lowered 5-hmc density leads to abnormal Hedgehog pathway expression involved in neural tube defects

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Objective
To investigate the mechanism about the folate deficiency reduced DNA methyltransferases TET2 expression to lowered 5-hydroxymethylcytosine (5-hmC) density and abnormal Hedgehog (HH) pathway expression in neural tube defects (NTDs).

Methods
In mouse embryonic stem cells (mESCs) cells, hydroxymethylated immunoprecipitation sequencing (hMeDIP) was detected 5-hmC distributions and gene expression in folate deficiency vs normal conditions. Transcriptome profile of mESC was detected by RNA sequencing (RNA-seq) technology in folate deficiency vs normal conditions. The mRNA level of Tet2 and Hedgehog pathway genes in the low folic acid diet and methotrexate (MTX)-induced NTDs mouse modle, mESCs with folate deficiency conditions were detected by RT-qPCR. The enrichment of 5hmc on Hedgehog genes promoter region was detected by 5hmc-qPCR in mESCs. Hedgehog and TET2 genes expression in the human NTDs samples were detected by Nanostring technology, and TET2 protein level was detected by Western blot.

Result
The transcriptome profile analysis of mESC results showed that the DEGs were mainly enriched in DNA and PRC2 methylated under folate deficiency conditions. We found that Folate depletion decreased the levels of DNA methyltransferases Tet2 in mESCs models. We also found that downregulation of TET2 gene were observed in both brain tissue of mouse and human NTD cases, and low protein level of TET2 were found in the corresponding NTDs samples with their maternal serum folate under low levels. We demonstrated that a decrease in 5-hmc downregulated expression of the neural tube closure-related Hedgehog pathway genes Ptch1, Gli2, SMURF1, CSNK1G3, HHATL, and PRKACA in mouse embryonic stem cells under folate deficiency conditions. Furthermore, downregulation of Hedgehog pathway genes was also observed in human NTD cases.

Conclusion
Our results indicate that folate deficiency contributes to the onset of NTDs by altering TET2 expression weaken 5-hmc density and subsequently affecting expression of neural tube closure-related Hedgehog pathway genes. This may be a potential risk factor for NTDs in response to folate deficiency.

关键字 Neural tube defects (NTDs), Tet2, 5hmc, Hedgehog pathway genes, folate deficiency

分类：10. Epigenetics Physical Activity 表观遗传学 运动
1735

HDAC Inhibitor Sodium Butyrate promote brain histone crotonylation alleviated hypoxic and ischemic brain injury in neonatal rats through gut-brain axis

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Objective: Neonatal hypoxic-ischemic encephalopathy (HIE) is a clinical syndrome caused by ischemia, hypoxia, asphyxia results from other damage. Among the Short chain fatty acids(SCFAs), butyrate constitutes an importantenergy source for colonocytes and its also acts as an epigenetic control of gene expression via inhibition of histonedeacet ylases (HDAC). This study explored how Sodium Butyrate (SB) as a Inhibitor of HDAC can alleviate hypoxic and ischemic brain injury in neonatal rats by regulating brain histone 3-lysine 9-crotonylation (H3K9cr).

Methods: We subjected 45 ten-day-old Wistar rats , were randomly divided into 3 groups of 15 rats each as Sham group, HIBD group and HIBD+SB group(SB 300 mg/kg, intragastric). Hematoxylin-eosin (HE) staining was conducted to evaluate pathological changes and the extent of brain damage. Western blot analysis of the level of brain tissue histone crotonylation in several groups. The localization and expression of H3K9cr in rat brain tissue was detected by immunohistochemistry. To explore how HDAC inhibitors SB alter the distribution of histone crotonylation over the genome, we used ChIP-seq and ChIP-qPCR analysis of H3K9cr.To evaluate the detailed alteration in gut microbiota, high-throughput sequencing of 16S rRNA was performed. The LC/MS non-targeted metabolomics were conducted for studying of correlation between the differentially expressed genes and the content of metabolites.

Results:HE staining results revealed that the neuron in Sham was better aligned and structured, in the HIBD group,the brain neuron tissue was atrophic and pale, with a thin cortex and the formation of a few voids. Furthermore, the neuron in the hippocampus in HIBD group had more cell death. In contrast, damage was substantially improved in the HIBD+SB group in comparison to the HIBD group. Western blot analysis of the level of brain histone modification in three groups using the antibodies against acetyl-lysine，crotonyl-lysine，malonyl-lysine indicates that the histone crotonylation was down-regulated in HIBD group and, interestingly, crotonyl-lysine(Includs H3K9cr) levels were found to be upregulated in HIBD+SB group. Expression of H3K9cr was detected by immunohistochemical staining, the data showed that the positive expression of H3K9cr in the infarct cortex in HIBD group decreased compared with sham control ($P<0.01$), while SB treatment up-regulated H3K9cr expression obviously compared with HIBD group ($P<0.01$). ChIP-qPCR for H3K18cr show a significantly increased H3K9cr/H3 level at BDNF gene promoter in response to SB mediated HDAC inhibition. The hypoxic-ischemic brain damage reduced the abundance of Lachnospiraceae and Clostridium bacterium in the fecal, while SB supplementation increased the abundances of Bifidobacterium, Lachnospiraceae, and Clostridium. Those bacterium were the most significantly promoted SCFA producers. Fecal metabolic profiling showed significant increases in metabolites involved in CoA biosynthesis , TCA cycle and butanoate metabolism was substantially reduced in the HIBD group compared with the Sham group.In the HIBD+SB group showed increased enrichment of ac-CoA precursor metabolites, such as Valeric acid and 3-Hydroxybutyric acid, and significantly increased N-Acetyl-L- Lysine related to epigenetic modification compared with that in the HIBD group. Pearson’s correlation

analysis shows that the Bifidobacterium and Lachnospiraceae were positively correlated with the abundances of Pyruvic.
Conclusion: HDAC Inhibitor SB changed the abundance/composition of the gut microbiota and significantly changed the fecal metabolic phenotype. HDAC-dependent H3K9cr epigenetic regulation was the reason for the alleviation of Hypoxic-Ischemic Brain Injury in neonatal rat. Regulating the gut microbiota and targeting restoration of these SCFA producers may present a novel ecological approach for managing HIE.

关键字 Sodium Butyrate; Hypoxic-Ischemic; histone crotonylation; gut microbiota;

Others

其它

分类：20. Others 其它
84

Summary and analysis of 228 children with special special health status

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Objective To summarize the characteristics and adverse reactions after vaccination of children with special health status, so as to provide clinical basis for the formulation of vaccination standard for special health status children. Methods the datas of 228 children with special health status visited the vaccination clinic of Guangzhou Women's and children's Medical Center in Guangdong Province from December 2020 to February 2021 were collected. The medical records, vaccination registration datas and adverse reactions of the special needs who consulted the immunization were retrospectively analyzed. Results 189 cases (82.89%) could be vaccinated according to the national immunization procedures, 27 cases (11.84%) could be vaccinated with inactivated vaccine according to the national immunization program, and 216 cases (94.74%) had no serious adverse reactions. Conclusion The vaccination clinic for special health status has effectively solved the problem of referral from vaccination, consultation and evaluation to clinical treatment. It is also an effective way to solve the problem of vaccination for special health status by setting up consultation and vaccination clinics for children with special health status, improved the vaccination rate of children with special health status, and made children with special health status getting more timely protection.

关键字 特殊健康状态儿童；疫苗；免疫接种

分类：20. Others 其它
88

The QCC was applied to improve the pass rate of the writing report of Neurophysic examination

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Abstract: Objective: Neurophysic examination is an important diagnostic basis for neurology diseases, and this study established QCC, which is used to improve the pass rate of nervous system specialty viewing and writing.
Methods: Using environmental intervention methods, the placement of items was standardized, and the number of companions was reasonably allocated to new patients.Doctor intervention methods, improve the importance of doctors to specialist examination, children and family intervention methods, the development of physical examination-related knowledge manual to let family members understand the importance of physical examination, institutional intervention methods, combing the physical examination process, the development of standardized procedures, training and learning of doctors, developing body-checking writing templates, and importing HIS systems.
Results: The pass rate of physical examination report was 6.03% at the beginning of the trial and increased to 68.25% during the trial after QCC was established.
Conclusion: The use of QCC improved the pass rate of writing reports of Neurophysic examinationto check the body, and provided a theoretical basis for the diagnosis of neurology diseases in the later stages.

关键字 QCC; Neurophysic examination;

分类：20. Others 其它
125

Aldehyde dehydrogenase 2 dysfunction in the early period is involved in the liver jury of vinyl chloride and high-fat diet

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Background: Vinyl Chloride (VC) is an industrial contaminant widely used in our daily life. It was found that people exposed to high-level of VC were more susceptible to steatohepatitis in the past few decades. We have shown that VC at low concentrations also exacerbates diet-induced liver injury in mice, mediated by mitochondrial dysfunction. However, the more detailed mechanisms remain elusive. Aldehyde dehydrogenase 2 (ALDH2) serves as a protective enzyme of removing reactive aldehydes, including chloroacetaldehyde. Previously, we have shown that ALDH2 activation by Alda-1 protect liver function in mice of VC+HFD. However, whether ALDH2 activity and expression is affected during the modeling period is unclear. In this study, we aim to determine the function of ALDH2 at different time point.
Methods: C57Bl/6J mice were exposed to VC via inhalation at concentrations below the current limit (<1 ppm), or room air for 6 hours per day, 5 days per week for 12 weeks. Mice were fed diets rich in saturated fatty acids (HFD: 42% fat), or a chow- diets as control groups. Some mice we administered ALDH2 agonist Alda-1 (i.p. 20 mg/kg, 3 times/week) for 3 weeks prior to sacrifice. At the time point of 6th , 8thand 12thweek, mice mitochondria were isolated for ALDH2 activity and expression measurement, plasma and liver samples were collected for histology and indices of inflammation, and liver damage.
Results: VC increased plasma transaminase activity in the HFD group at 8th and 12th week model, as determined by histologic indices of damage, this injury was characterized by enhanced steatosis, inflammation and necrotic cell death. However, in the 6th week modeled mice exposing to VC, plasma transaminase activity and degree of steatosis were significant higher in HFD feeding mice than that in chow diet group, while no noticeable difference of inflammation and necrotic cell death was observed between control diet +VC group and HFD +VC group. ALDH2 activation by Alda-1 decreased these effects in the mice of 12th modeled liver sample. In our model, we found that VC impaired ALDH2 activity at 6th、8th and 12th week in the HFD mice, but the expression in all the groups were varied from each other. ALDH2 expression was increased in 8th week and deceased in 12th week in VC+HFD groups comparing to the control mice, while no significant change was found in the 6th week.
Conclusion: Taken together, these results support that ALDH2 plays a critical role in protecting liver function in the mice exposing to low concentration VC and HFD. Importantly, ALDH2 also appears to be a direct target of VC exposure, which likely contributes to the enhancement of liver injury under HFD feeding, especially in the early period. These findings also suggest a potential therapeutic way for eliminating the risks of VC and HFD induced liver injury.

关键字 ALDH2; liver; vinyl chloride; high-fat diet

分类：20. Others 其它
234

EFFECT OF THE COVID-19 PANDEMIC ON THE STATUS OF OVERWEIGHT AND OBESITY AMONG CHILDREN AND ADOLESCENTS: A RETROSPECTIVE STUDY IN CHENGDU, CHINA

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Background: Overweight and obesity among children and adolescents have become a public health concern. Lifestyle changes due to the COVID-19 pandemic may have an impact on the status of overweight and obesity among children and adolescents. This study aimed to analyze the effect of the COVID-19 pandemic on the status of overweight and obesity among children and adolescents.
Methods: We retrospectively analyzed the children and adolescents who visited the West China Second University Hospital, Sichuan University from January 1st, 2018 to June 30st, 2020. We divided the obesity children into 5 groups and chose the national lockdown time as a segmentation point.
Results: A total of 140,526 children and adolescents visited the outpatient department during the study period, and 1,740 of them were diagnosed as overweight or obese. There was a difference in the obesity rate among the groups ($P < 0.01$). However, there was no difference between January to June, 2020 and the previous period. Except for the increased incidence of VD deficiency($P < 0.01$), the severity of obesity, insulin resistance and dyslipidemia of obese children did not change($P=0.303$, 0.663, 0.106, respectively). A total of 65 obese children were followed up before and after COVID-19 lockdown. There were no significant differences in BMI-SDS, HOMA-IR and 25(OH)VD among them ($p = 0.626$, 0.386, 0.251, respectively).
Conclusions: The available evidence cannot prove that the COVID-19 pandemic affects the status of overweight and obesity among children and adolescents who visited hospitals.

关键字 COVID-19 pandemic , childhood obesity, Insulin resistance, VD deficiency, Dyslipidemia

Category: 20. Others 其它
268

THE EFFECT OF CUP FEEDING ON THE DURATION OF EXCLUSIVE BREASTMILK FEEDING IN HEALTHY TERM INFANTS DELIVERED AT A PRIVATE TERTIARY HOSPITAL: A RANDOMIZED ENCOURAGEMENT TRIAL

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Abstract Content Background: The primary objective of the study is to determine if encouragement to cup feed will prolong the duration of exclusive breastmilk feeding for 6 months.

Methods A randomized encouragement trial was used to determine if cup feeding is an effective way to prolong exclusive breastmilk feeding up to 6 months. A randomized encouragement trial is a variation from the classic randomized control trial and this study design is useful for interventions for which it is unethical to require adherence.[1] Healthy term newborns delivered at a private tertiary hospital by mothers who were on maternity leave, mothers who had difficulty latching, and mothers who experienced nipple pain were included in the study. Participants in the study were randomly assigned using the Fishbowl draw method to the Encouragement to Cup Feed Group and No Encouragement to Cup Feed Group. Participants in both groups were followed up monthly for 6 months.

Results A total of 261 participants were included in the study. 131 participants were in the Encouragement to cup feed group and 130 participants were in the No Encouragement to cup feed group. Chi square test for proportions was used to determine the significant difference of the results of the frequencies and percentages of cup feeding and exclusive breastfeeding rates. Exclusive breastfeeding rates among those who are encouraged to cup feed are significantly higher during the first, second, and fourth month of follow-up (47.9%, 80.4%, and 80%) compared to those who are not encouraged to cup feed (30.8%, 57.1%, and 41.7%). Exclusive breastfeeding rates among those who are cup feeding during the first and second month of follow-up are 78.3% and 94.7% compared to 35% and 65.3% among those who are not cup feeding but did not significantly increase the exclusive breastfeeding rates during the third to sixth month of follow-up.

Conclusion Encouragement did not increase the cup feeding rate. Encouragement increased the breastfeeding rates on the first, second, and fourth month of follow-up. Cup feeding increased the exclusive breastfeeding rates compared to encouragement alone but only during the first two months of follow-up.

Key words randomized encouragement trial, cup feeding, breastfeeding, breastmilk

Reference 1. West, S., Duan, N., Pequegnat, W., Gaist, P., Des Jarlais, D., Holtgrave, D.,…Mullen, P. (2008). Alternatives to the Randomized Controlled Trial. American Journal of Public Health, 98(8), 1359-1366

分类：20. Others 其它
277

The anti-tumor role and mechanism of rMV-Hu191 in esophagus cancer

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Esophageal cancer is highly malignant with poor prognosis, and there are currently no effective treatment especially for advanced or metastatic esophageal cancer. Oncolytic virus therapy is a promising new therapeutic approach for cancer treatment. Oncolytic virus specifically replicate in tumor cells and ultimately destroy the tumor without harming the normal tissues. Oncolytic measles virus therapy has been shown to have significant antitumor activity in recent years. In our previous study, we have found that the recombinant oncolytic measles virus rMV-Hu191 has a strong killing ability on human esophageal squamous cell carcinoma cells. In this study, we try to find the key factors for the anti-tumor activity of rMV-Hu191 in ESCC by using molecular biochemical methods combined with mouse models in order to provide a new theoretical basis and clinical treatment strategy for esophageal squamous cell carcinoma

关键字 recombinant measles virus; rMV-Hu191; anti-tumor; esophagus cancer; cell death

分类：20. Others 其它
297

On Issues in Pre-examination and Triage of Out-patient and Emergency Departments of Pediatrics and Its Countermeasures

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[Abstract] Purpose: this paper studies and analyzes issues in hierarchical diagnosis and treatment of pediatric outpatient department and finds solutions. Methods: the study objects refer to 170 child patients in pediatric clinic from March 2015 to October 2015, and they are divided into control group and observation group by means of random number table, with 85 child patients in each group. In control group, the patients are treated with conventional treatment mode, while patients in the observation group are treated with grading diagnosis and treatment so as to observe satisfaction of family members in two groups and children's recovery as well as contrast difference of accident times during treatment; finally, the appropriate measures are taken to address issues. Result: The current situation of pediatrics is that the number of children in emergency is much, and the family members are more irritable. Among them, children in critical and urgent situations often appear in a mixed way. They are treated simply according to the order of seeking medical treatment, which is easy to delay the best rescue time for children who really need emergency treatment and delay the disease. conclusions: Pediatric outpatient and emergency classification and treatment need to establish a consensus and be standardized, institutionalized and humanized to establish regulations. Then it is widely promoted and used in clinical practice, but the problems arising in the process of grading diagnosis and treatment also need to be solved constantly.

关键字 [Key words]: Hierarchical Diagnosis and Treatment; Pediatric Department; Issue and Countermeasures

分类：20. Others 其它
298

Medical behavior and medical psychology Analysis of the Stress Status of Pediatric Professional Technical Team in One Hospital, Shanghai

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Abstract: Objective: To analyze the pressure status of pediatric professional technical team in one hospital, Shanghai and to offer suggestions for the construction of pediatric technical team. Methods: the study objects refer to 115 pediatric doctors and nurses in one hospital, Shanghai from January 2014 to December 2014; work stress of pediatric medical staff is surveyed through self-made clinical stress questionnaire in hospital, and the business examination is carried out to test business level of staff. Results: the stress degrees of pediatrician and nurse are 3.02 ± 0.87 and 3.67 ± 0.79 respectively, which are significantly higher than the average level in this hospital (P <0.05); the stress degrees of pediatric nurses are significantly higher than that of pediatrician (P <0.05). There is no statistical significance for difference in academic stress between pediatricians and nurses (P> 0.05). The academic stress for pediatric nurses is higher than that of pediatricians, which means the difference is of statistical significance (P <0.05); medical staff feel the highest stress on doctor-patient relationship (3.01 ± 0.93); the business examination is general for pediatric professional staff (61. 07 ± 6. 18 scores), and wherein, doctor's score is (64.28 ± 7.89), a figure which is higher than that of nurses (57.32 ± 8.12), indicating that the difference is of statistical significance (P <0.05). Conclusion: in construction of pediatric professional technical team, there are issues existed such as intense stress of working staff, strained doctor-patient relationship and the lack of professional qualifications; therefore, it is suggested that measures should be taken to rationally allocate medical staff, strengthen communication between doctor and patient, and improve business qualifications of professional staff.

关键字 Key words: Pediatrics; Professional technical team; Stress condition

分类：20. Others 其它
299

Analysis on the Mode that Pediatric Department Guides and Teaches General Practitioners on General Hospital

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[Abstract] The difficulty of getting medical service is a serious problem that China faces for long term; what's more, there are also sufficient medical resources, uneven distribution of superior resources, especially, pediatric medical resources have too many problems to deal with. Thus, through taking tertiary general hospital as core, we construct regional medical treatment alliance, implement hierarchical diagnosis and treatment, send superior resources to communities, and make specialist physicians connect with general practitioner to remit the severity of this problem. In this text, we make exploration and research on the mode of pediatric department training and general practitioner's pediatric skills retraining, and its aim is to make efforts to train general practitioners and makes contribution to the development of basic health protection and remission for the difficulty of getting medical service in each level of hospitals.

关键字 General Hospital; Pediatric Department; Guidance and Teaching; General Practitioner

分类：20. Others 其它
300

Applied Analysis of Improving Grassroots Pediatric Service Skills with Medical Alliance Mode

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[Abstract] Objectives: The medical alliance mode rises in response to the insufficient medial resources and uneven distribution of quality medial resources in China. However, it is worth-noticing that few hospitals have carried out cooperation in specialty medical sciences, especially in pediatric diagnosis and treatment. The flourishing of children is vital to the future of our country. At the same time, grassroots hospitals, as the hub of medical and health service network in rural areas, play a vital role in medical and health service system. In light of the weak diagnosis and treatment service skills of doctors from grassroots hospitals, this paper probes into the application effect of medical alliance model to the improvement of grassroots pediatric service skills. Methods: By means of document research and case analysis methods, this paper took a community health service center as the example and analyzed the teaching effect of general practitioner in pediatric department through the platform of medical alliance. Results: The number of children patients increased from 50 every month to almost 150.
Conclusions: In the future medical system, general practitioners will shoulder the responsibility of basic medical services. Therefore, effective measures should be taken to constantly enhance the clinical skills of general practitioners, build up a high-quality pediatric diagnosis and treatment team and promote the establishment and development of hierarchical medical system. In this sense, carrying out the specialty training for general practitioners under the medical alliance mode is of great importance to improve the pediatric service skills.

关键字 Medical Alliance Mode; Grassroots; Pediatric Diagnosis and Treatment; Service Skills
分类：20. Others 其它
345

Improvement of co-train professional ethics model for Chinese pediatricians By Entrustable Professional Activities.

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Medical development has been a worldwide subject of research. Scholars in various countries have made numerous explorations on root causes of medical problems. The World Health Organization (WHO) introduced a basic framework on integrated health service system in 2016 and made it a global health strategy contributing sustainable development goals. In the same year, Chinese government, World Bank and WHO launched a joint research report, in which a people-centered integrated health service plan was proposed and practices were made subsequently. Considering the scarcity of medical resources in China, the gap between eastern China and Western China and that of the supply and demand, lacking of sound ground-level medical systems, the 19th National People's Congress of the Chinese Communist Party put forward the goal of building a comprehensive medical service system that is of high efficiency, good quality and Chinese characteristics. There are many contributors to medical accessibility and affordability issues in China, for example, big workload for specialist physicians, insufficient supply of general physicians, patients' preferences for tertiary hospitals, etc. In this research, a job competence theory and entrustable professional activities theory are employed to explore a training model for Chinese pediatricians via qualitative and quantitative analysis. The model can be used for the further education for Chinese pediatricians and pediatric skill training for general physicians, .

We opted for a mixed methods approach as it offers the possibility of joining the strengths of both qualitative and quantitative). building on the meaning individuals bear while allowing for a situated understanding of phenomena, namely its context dependency.it may compromise external validity in the sense that findings may not extrapolate to general settings other than the context it came from and it is more likely that the personal biases of the researcher influence results Quantitative approach is more suitable to generalize research findings and test hypotheses with minimal interference of the researcher's expectations and biases while allowing for the quantitative predictions of phenomena controlling for confounding effects of other variables. It is however more probable that a priori hypotheses may not reflect the true latent representations of concepts or phenomena and thus it may fail to grasp the most important dimensions of a phenomenon in interdependence with its context. It is also frequent that papers report convenience sampling although dealing with findings as if random sampling was in place. That can promote an inflated sense of representativeness that is not truly observed.

Thus, mixed methods are particularly suitable to deal with complex domains of which health is a good example. This is probably a reason why research in health sciences has been keen on these methods .

In designing this mixed methods study, we considered both explanatory and exploratory sequential designs . As our major intention was exploratory in nature we were motivated firstly to uncover freely generated interpretations of EPA in pediatrics in China, we deployed the exploratory sequential design from the perspective of an inductive approach. With the insight it provided from qualitative data analysis we

are able to design a questionnaire that allows for a comprehensive data collection, thus integrating all variables into a single explanative model.
From this stage it was shown that the more complex the medical practice, the less the ethical influence, and the more the primary medical practice, the stronger the ethical influence, so that in the early general practice and community medical settings, the display of ethical and medical behavior is the highest. It is suggested that doctors should pay attention to humanistic feelings in the early stage of medical treatment, which will improve patients' satisfaction and happiness.

关键字 Keywords:EPA (Entrustable Professional Activities), Medical education, Pediatricians, Training; professional ethics;

分类：20. Others 其它
361

Comparison of the STAMCO and EAONO/JOS and ChOLE Cholesteatoma Staging Systems in the Prognostic Evaluation of Pediatric Middle Ear Cholesteatoma

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Abstract
Objective
To compare the performance of STAMCO Classification and EAONO/JOS and ChOLE Cholesteatoma Staging Systems in prognostic evaluation of pediatric middle ear cholesteatoma after primary surgery and identify the specific predictors for cholesteatoma recidivism.
Methods
A total of 173 patients who underwent surgery for primary cholesteatoma from November 2008 to July 2020 were included in this retrospective study, and then classified and staged according to the STAMCO classification, EAONO/JOS staging system and ChOLE cholesteatoma staging system. The association between different stage and recurrence in each system was assessed respectively.Each indicator involved in the system was analyzed separately to evaluate its prognostic value for cholesteatoma recurrence.
Results
Eroded long process of the incus (p=0.017) and CWU surgery (p=0.020) were identified to be associated with an increased risk of cholesteatoma recidivism. No association was found between complications and recidivism rates. When focusing on the CWU operation group, ossicular chain status-O2 in STAMCO stage (p=0.018) and O2 in ChOLE stage (p=0.006)-were significantly associated with cholesteatoma recidivism.
Conclusions
Based on our study, the STAMCO classification shows more significant performance than the other two systems for predicting cholesteatoma recidivism. Additional validation studies are entailed to definitively assess the clinical utility of these classifications.

关键字 Cholesteatoma, EAONO/JOS, STAMCO, ChOLE, staging, classification, recidivism, children
分类：20. Others 其它

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Quality and consistency of clinical practice guidelines for treating children with COVID-19

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Background
The Coronavirus Disease 2019 (COVID-19) pandemic negatively affects children s health. Many guidelines have been developed for treating children with COVID-19. The quality of the existing guidelines and the consistency of recommendations remains unknown. Therefore, we aim to review the clinical practice guidelines (CPGs) for children with COVID-19 systematically.
Methods
We systematically searched Medline, Embase, guideline-related websites, and Google. The Appraisal of Guidelines for Research and Evaluation II (AGREE II) tool and Reporting Items for practice Guidelines in HealThcare (RIGHT) checklist were used to evaluate the methodological and reporting quality of the included guidelines, respectively. The consistency of recommendations across the guidelines and their supporting evidence were analyzed.
Results
Twenty guidelines were included in this study. The mean AGREE II score and mean RIGHT reporting rate of the included guidelines were 37% (range, 22 62%) and 52% (range, 31 89%), respectively. As for methodological quality, no guideline was classified as high, one guideline (5%) moderate, and 19 (95%) low. In terms of reporting quality, one guideline (5%) was rated as high, 12 guidelines (60%) moderate, and seven (35%) low. Among included guidelines, recommendations varied greatly in the use of remdesivir (recommend: 25%, not recommend: 45%, not report: 30%), interferon (recommend: 15%, not recommend: 50%, not report: 35%), glucocorticoids (recommend: 50%, not recommend: 20%, not report: 30%), and intravenous immune globulin (recommend: 35%, not recommend: 30%, not report: 35%). None of the guidelines cited clinical trials from children with COVID-19.
Conclusions
The methodological and reporting quality of guidelines for treating children with COVID-19 was not high. Recommendations were inconsistent across different guidelines. The supporting evidence from children with COVID-19 was very limited.

关键字 Clinical practice guidelines; quality appraisal; Coronavirus Disease 2019

分类：20. Others 其它

786

Research and development of COVID-19 vaccine based on live attenuated mumps vaccine

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Purpose: Since 2019, COVID-19 has spread the world and brought serious health threats to people all over the world. The most effective way to prevent COVID-19 is to develop an efficient, safe and durable vaccine. Method: Using live attenuated mumps vaccine virus (S79 strain) as a vector, a recombinant COVID-19 vaccine expressing a specific antigen protein of SARS-CoV-2 was developed. According to the genes of the SARS-CoV-2 epidemic strain announced by NCBI, intercept the spike protein, subunit protein S1 of spike protein and receptor binding domain-RBD protein genes, we synthesis above genes, then use specific PCR amplification, seamless cloning connection methods to insert these target genes to the full-length cDNA of mumps virus.The recombinant mumps virus vaccine strains carrying the S protein, S1 protein, and RBD protein was rescued by our laboratory's efficient reverse genetics system and virus rescue system. The safety and immunogenicity experiments of recombinant mumps virus vaccines were tested on two animal models-IFNα-/γ-receptor knockout mice. Results: The spike protein gene of the epidemic strain of SARS-CoV-2 was successfully synthesized, and the mumps virus full-length cDNA clone carrying the S protein, S1 protein and RBD protein was successfully constructed, and the recombinant mumps virus that successfully expressed the above genes was rescued successfully. Viral RNA reverse transcription, second-generation sequencing, Western blot, immunofluorescence and other methods have identified the foreign gene protein expression of the above viruses. In animal experiments, the safety of recombinant virus vaccine strains in mice was tested, and it was verified that three recombinant virus vaccine strains carrying SARS-CoV-2 antigen genes stimulated animals to produce SARS-CoV-2 neutralizing antibodies to varying degrees. Discussion: Mumps live attenuated vaccine has a history of more than 60 years of vaccination in my country. It has high safety, mature production system, and can insert and express longer foreign genes, but it is aimed at the high mutation rate and high transmission of COVID-19. Efficiency. Although the above three vaccine strains can stimulate animals to produce different levels of neutralizing antibodies, the protection efficiency may not be very optimistic. Therefore, how to select efficient antigen genes and better prevent the spread of COVID-19 has become the focus and difficulty of this experiment.

关键字 mumps virus、COVID-19、spike

Category: 20. Others 其它

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THE USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) AMONG PEDIATRIC EMERGENCY AND OUTPATIENT DEPARTMENT PATIENTS AT A PRIVATE TERTIARY HOSPITAL

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Abstract Content This study aims to determine the prevalence and pattern of Complementary and Alternative Medicine (CAM) use among pediatric patients presenting in a private tertiary hospital.

Methods This is a descriptive, cross-sectional, prospective study. One hundred thirty-eight pediatric patients seen at the outpatient and emergency department were randomly selected. Eligible patients are 0-18 years old, medically stable, and without cognitive impairment. Excluded are those who are critically ill. The sample size was determined using the Slovin's Formula based on the average number of yearly pediatric admissions at the private tertiary hospital. A 28-item questionnaire used in an adult study was validated and used. There were no drop-outs in this study. There were no interventions done.

Results Sociodemographic characteristics of CAM users were examined. More than 50% of CAM users belong to 5 years old and below, predominantly females and Filipinos from the outskirts of the city. Eighty-three percent are Roman Catholic. Parents are the primary caregivers (62%) and are college graduates (70%) and professionals (68%). Sixty percent have an insurance plan and 96% are sick. Fever is the main presenting complaint while massage and liniments the most common CAM used. CAM is perceived effective however significantly less compared to conventional drugs. CAM offers personalized treatment, is readily available and greatly influenced by Filipino culture. It is usually recommended by relatives. Many patients are not discussing CAM use with their physicians thus increasing the likelihood of adverse drug interactions.

Conclusion CAM use is high among pediatric patients in the outpatient and emergency department of a tertiary hospital in the province. Most respondents perceive it as effective despite being less than conventional medicines.Promotion, research and standardization practices on CAM are highly recommended.

Key words complementary medicine, alternative medicine, traditional medicine, CAM, pediatrics

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分类：20. Others 其它

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Intracerebroventricular injection of RF9 stimulates luteinizing hormone secretion but does not advance puberty onset in young female rats

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Background: RFRP-3 has long been identified as inhibitors of the hypothalamus-pituitary-gonad (HPG) axis in mammals. A large number of studies have suggested RFRP - 3 can inhibit LH release in adult mammals by combining into the G protein coupled receptor 147 (GPR147) and affect the function of reproductive system. However, there is little evidence documenting whether RFRP-3 plays a primary role in inhibition of the HPG axis prior to the onset of puberty. RF9 is antagonist of RFRP-3 receptor (GPR147). Our study aims to explore the possible function of this neuropeptide on pubertal development in young female rats by injecting RF-9 intracerebroventricularly.
Methods: 18 female rats were randomly divided into normal group(N), vehicle contrast group(NS), RF9 group on postnatal day 21. Each group consisted of 6 female rats and animals were fed and kept separately one from another in single cage. On postnatal day 22, we implanted cannulas into the lateral ventricles of female rat pups. From postnatal day 28 to postnatal day 36, the intracerebroventricular injection of RF9, or vehicle, was conducted twice a day. To investigate whether puberty onset was affected, we examined the serum luteinizing hormone(LH) and growth hormone(GH) levels, age of vaginal opening (was generally believed an essential symbol of puberty onset), uterus and ovary development, and hypothalamic Kiss-1, GnRH mRNA expression.
Results: Level of serum LH was significantly higher in group RF9 (39.21±2.91mIU/ml) than those in group NS (29.53±1.74ug/ml; P=0.002). But, intracerebroventricular injection of RF9 did not accelerate uterine and ovarian maturation, and not make the time of puberty onset earlier. The time for vaginal opening in group RF9(29.50±1.23d) comparing with group NS (30.00±0.89d; P>0.05) showed no significance. RF9 does not affect the levels of Kiss-1 and GnRH mRNA. Moreover, our data show that the levels of serum GH were significantly lower in group RF9(10.72±2.02 ug/ml) than those in group NS (29.53±1.74ug/ml, P=0.000).
Conclusions: These data suggest that intracerebroventricular injection of RF9 stimulates LH secretion but does not advance puberty onset in young female rats. It may indicate that RF9 directly affects the secretion of LH in the pituitary, not by acting on Kiss-1 neurons or GnRH neurons in the hypothalamus. Additionally, RF9 may be associated with prepubertal decline in the secretion of GH.

关键字 RF9, RFRP-3, LH, Puberty onset, Kiss-1

分类：20. Others 其它

1115

Indication Alerts Intercept Medication Errors in Pediatric Inpatients by Prescription Pre-audit Intelligent Decision System

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ABSTRACT
Objective Medication errors in hospitals may occur at any stage of the patient's stay. Research is needed to demonstrate pharmacist value and their roles in pediatric patient therapy.
Methods This descriptive retrospective study was conducted on pediatric hospital. Grade 7 medical orders intercepted by the Prescription Pre-audit Intelligent Decision System in Jan. 1st 2019 to Dec. 31st 2020, and the Intercept Medication Errors in pediatric patients age, department distribution, drug classification, drug dosage forms, route of medications and the types of errors were analyzed by excel.
Results A total of 2176 medication errors and the most common medication errors were drug dosage error, incorrect route and frequency, accounting for 35.2%, 32.8% and 13.3%, respectively. The intercept medication errors were mainly injection (50.4%), topical solutions (19.5%), tablet (9.1%) and inhalation (5.7%), and the routes of administration were mainly intravenous, oral routes and external use. The drugs that intercepted medication errors were mainly anti-infection drugs, and most common in neonatology department (including NICU), nephrology department and PICU, with the incidence rates of 40.5%, 15.9% and 11.3%, respectively.
Conclusion The most frequent medication errors were wrong dosage, administering the medication to patient, and frequency in pediatric inpatients. The Prescription Pre-audit Intelligent Decision System can reduce the incidence of medication errors in hospitalized children and improves the clinical rational drug use in the hospital. It is a medical service model worthy of consideration.

关键字 Keywords: pediatrics; rational medication use; database; prescription pre-audit; intelligent decision

分类：20. Others 其它

1120

Piloting multiple value framework and decision approaches of drug selection for policymakers: A multi-criteria decision analysis applied to generic medicine ranking

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Background: China has 189,000 drug production approved, of which 95% are generic medicine. While the popularity of low-cost generics has brought cost savings to the health system, there are huge differences in efficacy, safety, and price among them. A comprehensive evaluation strategy based on Multi-criteria decision analysis (MCDA) is proposed to select these drugs. Methods: In this study, an MCDA model was developed to appraisal alternative drugs. This model employed an integrated approach of the analytic hierarchy process (AHP) which contains four parts: the goal for drug ranking, the value framework of the drug for judge, computing module based on Entropy weight (EW) plus technique for order preference by similarity to ideal solution (TOPSIS) methods and the data of candidate drugs. Real-world data from designated hospitals collaborations inform the process of the model. The utility score is obtained through the model. The higher the utility score, the better the drug. Results: The value framework for medicine consists of six criteria: safety, efficacy, disease burden, innovation, adaptation, and accessibility. For efficacy and safety, their sub-criteria were derived from a literature review after GRADE guideline evaluation, which was then confirmed by expert surveys. Disease burden refers to the cost of medicine, adjuvant treatment, and other losses incurred in-hospital treatment. Innovation, adaptation, and accessibility, we use a rating scale. Data are provided by pharmaceutical companies or obtained through market research. By using the EW-TOPSIS method, we obtain 6 ideal closeness degree scores (range 0-1) for each candidate drug. Then, a decision-maker weight questionnaire for each criterion was conducted by a leading group of decision-makers, then these scores were summarized using an additive model. Conclusion: The MCDA process has the potential to support better healthcare decision-making, which deconstructs complex drug policy issues into a set of simpler judgments that led to consensus about the results. We for the first time shown how MCDA can be used when making a selection of an optimal medicine. This comprehensive approach can help decision-makers, clinicians, and related researchers to better understand how a generic drugs assessment can be conducted. Besides, leadership groups, the collaboration of hospitals and data resources are essential.

关键字 drug use; medicine; evaluation; multi-criteria; ranking

分类：20. Others 其它

1188

Pediatric clinical trials in mainland China over the past decade (from 2009 to 2020)

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Abstract

Background: Like most areas worldwide, there is a shortage of pediatric drugs in mainland China to provide prescriptions. The Chinese government recently launched policies and incentives to encourage pediatric drug development and clinical trials. However, few data are available on the characteristics or development trends of these trials.

Methods: We extracted source data from the Chinese Clinical Trials Registry and Information Transparency Platform and systematically reviewed the pediatric clinical trials conducted in mainland China from 2009–2020, providing data support to policy makers and industry stakeholders. This study includes 487 pediatric clinical trials.

Results: Over the past decade, the number of pediatric trials has increased annually, especially since 2016. The most common therapeutic areas were infectious diseases (n = 108, 22.2%), agents for preventive purposes (n = 99, 20.3%), and neurological and psychiatric diseases (n = 71, 14.6%). The number of clinical trials involving epilepsy (39, 10.1%), asthma (33, 8.5%), and influenza (24, 6.2%) were the highest. The distribution of leading institutions is unbalanced in mainland China, with most units in East China (34.0%) and few in Southwest China (6.9%). China has made constant progress in improving the R&D environment of pediatric drugs and increasing pediatric trials. However, a wide gap in pediatric drug development remains between China and developed countries.

Conclusions: The pharmaceutical industry in China still faces grim setbacks, including study duplication, a lack of innovation, and poor research design. Thus, the Chinese government should adjust their policies to improve innovation and clinical design capacity, and to optimize resource allocation between regions.

关键字 pediatric clinical trials, National Medical Products Administration (NMPA), Chinese Clinical Trials Registry and Information Transparency Platform (CCTR and ITP), pediatric population, drug research and development

分类：20. Others 其它

1244

Switching between LC-ESI-MS/MS and EMIT methods for routine TDM of Valproic Acid in Pediatric patients with epilepsy: What Clinicians and Researchers Need to Know

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Background: Valproic acid (VPA) is a widely used antiseizure medication and its dosing needs to be individualized through therapeutic drug monitoring (TDM) to avoid or prevent toxicity. Currently, immune-enzymatic assays such as Enzyme Multiplied Immunoassay Technique (EMIT), and Liquid Chromatography (LC)-based techniques, particularly coupled to Electrospray Ionization Tandem Mass Spectrometry (LC－ESI-MS/MS), resulting a potential lack of concordance between laboratories.

Methods: In this study, 782 blood samples were collected from 711 children with epilepsy. All samples were collected between March and May 2021. The blood specimens were centrifuged, and the resulting plasma were analyzed immediately for a routine EMIT assay. The left-over plasma samples were separated and stored at -20° C until further LC-ESI-MS/MS analysis. The LC-ESI-MS/MS method was validated for selectivity, linearity, lowest limit of quantitation (LLOQ), intra- and inter-day accuracy and precision, recovery, matrix effects, stability and carryover. The study aimed to address the aforementioned concern. Consistency between two methods was evaluated using linear regression and Bland-Altman analysis.

Results: In the study, 782 plasma samples were measured by EMIT assay and then by LC-ESI-MS/MS method. Among those, 8 samples were below the LLOQ and were excluded from further statistical analysis. The calibration curve was linear in the range of 5.00-300 μg/mL for LC-ESI-MS/MS method and 1.00－150 μg/mL for EMIT assay, respectively. The two methods were proven to be accurate with quality control samples. As a result, a significant correlation between two methods was obtained with a regression equation described as following: [EMIT] = 1.214 × [LC-ESI-MS/MS] + 3.054, (r2 = 0.9281). VPA concentrations measured by LC-ESI-MS/MS and EMIT were 5.13 - 126 μg/mL (median 51.8 μg/mL) and 6.00 - 154 μg/mL (median 66.2 μg/mL), respectively. The median concentration of the plasma VPA determined by EMIT assay was 127.8% of results obtained from LC-ESI-MS/MS method. Bland-Altman plot showed a mean bias of 14.5 μg/mL (95% confidence interval (CI): [-0.2, 29.2]) and a mean increase of 27.8% (95% CI: [3.3, 52.4]) measured by EMIT assay more than that measured by LC-ESI-MS/MS method. In general, the results demonstrated a systematic overestimation of plasma VPA levels by EMIT with respect to LC-ESI-MS/MS values.

Conclusions: This is the first study to compare the plasma concentration of VPA measured by routine EMIT assay and thereafter by a novel LC－ESI-MS/MS method using a large number of pediatric blood samples (n=774). In conclusion, two methods were closely correlated, but EMIT assay overestimate VPA levels of 27.8% in human plasma compared with LC-ESI-MS/MS method, supporting the switch from EMIT to LC－ESI-MS/MS for routine TDM purpose. So far, LC-MS/MS has served as a widespread and efficient technique in many clinical laboratories for monitoring of different medications. Considering the observed significant discordance between EMIT and LC-ESI-MS/MS, switching from immunoassays to LC-based techniques for TDM of VPA deserves close attention and therapeutic range of 35.0－75.0 μg/mL may be feasible. Clinicians should be informed when switching the VPA quantitation methods during the clinical practice.

关键字 Valproic acid; LC-ESI-MS/MS; EMIT; Switch; TDM; Antiseizure medication

分类：20. Others 其它
1408

A gold nanosensor combined droplet microfluidic platform for rapid detection of single neuroblastoma circulating tumor cell

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Purpose

Neuroblastoma (NB) is the most common extracranial solid tumor in children. It has one of the lowest survival rates among all childhood cancers. Hematogenous metastasis is prone to occur in the early stage of NB. Circulating tumor cell (CTC) plays an important role in hematogenous metastasis, and becomes a new marker for early diagnosis of tumors. The purpose of work is to first develop a gold nanosensor to in situ detect the expression of the specific biomarker CD56 of living NB CTCs. Then to establish a microfluidic chip to fast separate the CTCs from blood samples to single-cell. Fluorescence from CD56 of single CTC can be detected and used for counting. We aimed to report a non-invasive sensing techniology with high efficiency and low cost to detect the CTCs from blood sample of children at different NB and conveniently reflect the treatment effect and prognosis of the patients.

Methods

1) A Fluorescent Resonance Energy Transfer (FRET) nanosensor for CD56 detection were established by using the fluorescence graphene quantum dots (GQD) as the donor, and gold nanoparticles (AuNP) as the acceptor. Biocompatibility of both nanoparticles to NB cell line SH-SY5Y were evaluated via MTT. The aptamer Tx-01 with good affinity to CD56 were modified with AuNP and GQD on both terminals, Due to the close distance between AuNP and GQD, green fluorescence of GQD can be quenched by AuNP by FRET, as a “turn-off “signal. In presence of CD56, the good affinity between CD56 target and aptamer made a steric hindrance and trigger the fluorescence recovery, as a “turn-on” signal. 2) A microfluidic chip was fabricated with u-shape and arc-shape channels. The cells were separated from each other by going through the channels and then dispersed in the ejection port to form single cell droplets. 3) SH-SY5Y cells were incubated with the nanosensor for 4 h at 37 ℃ and then the cell suspension with density of 5×10^5 cells/mL was used to test the generation of single-cell droplets. The fluorescence of each droplet was obtained with filters at 532nm. Then peripheral blood samples from the patients at the initial stage III and IV without treatment and after two courses of chemotherapy were collected and tested with same method above. All research operations comply with the relevant regulations of ethics.

Results

1) For the FRET nanosensor, the prepared GQD was the donor with strong fluorescence with emission peak at 521 nm, and AuNP was the acceptor with excellent optical absorbance from 300 -700 nm which can quench the GQD fluorescence. Both AuNP and GQD had high cell viability to SH-SY5Y cells of 94.67% and 97.13%, respectively. The limit of detection (LOD) of this gold nanosensor was determined by three times of the standard deviation of noise. LOD of the nanosensor for CD 56 detection was around 440 pM. 2) The microfluidic chip showed single cell parcel rate around 29.65%, empty droplet rate around 65.27%, and double-cell parcel rate around 5.08%. This chip can rapid encapsulate single-cell in one droplet at a speed of 2.89×10^3 droplets/min 3) With the high speed of single cell encapsulation, the fluorescence from CD56 of each single cell can be quickly quantified at the speed of 1×10^4 droplets/min. In 9 cases of stage III and IV NB, CTCs were detected in 6 cases of them with positive rate at 66.7%. After two courses of chemotherapy, CTCs numbers of the all 6 cases

decreased. In 1mL of real peripheral blood sample, there are about 5×10^8 normal blood cells and only 1-10 CTCs. The fast single cell separation and counting ability of this platform has important value in the clinical detection of a large number samples.
Conclusion
In this work we reported a novel nanosensor combined microfluidic chip (NCMC), in which NB CTCs of clinical blood samples were rapidly counted, the specific biomarker CD56 of NB CTCs were in situ detected in living cells. This platfrom showed good potential for early diagonsis of NB in clinics.

关键字 Neuroblastoma, Circulating tumor cell, CD56, Nanosensor, Microfluidic chip

分类：20. Others 其它
1540

Duchenne Muscular Dystrophy with Decrease of Acidic α-glucosidase Activity: Two Cases Report and Literature Review

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Background: Pompe disease is usually considered in children who repeatedly exhibit elevated creatine kinase and decreased acidic α-glucosidase (GAA) activity. However, there are exceptions because of the pseudo deficiency polymorphism variants, which can cause low GAA activity but do not result in disease. Here, we report two cases presenting increased creatine kinase and decreased GAA activity but ultimately diagnosed with Duchenne muscular dystrophy (DMD).
Case presentation: Case 1 was a 2-month-old boy who presented with a significant increase in creatine kinase (CK 5480~11880U/L). His activity of GAA in peripheral blood (colorimetric method) was 2.72nmol/1h/mg (reference value > 14 nmol/ 1h/mg). But the whole exome sequencing did not find the pathogenic mutation of GAA gene and instead find a DMD gene hemizygous variation (c. 7657C>T, p. Arg2553Ter) inherited from his mother, which was verified by the first-generation sequencing. However, further genetic analysis of GAA revealed two homozygous pseudo deficiency alleles (c.1726G>A, p. Gly576Ser and c.2065G>A, p. Glu689Lys), which explained the patient's low GAA activity. Therefore, the boy was diagnosed with DMD despite his remarkable reduction in GAA activity. Case 2 was also a 2-month-old boy presenting with significant increase in creatine kinase (CK 12408~24828U/L). His GAA activity in peripheral blood (colorimetric method) was 9.02nmol/1h/mg. Similarly, his whole exome sequencing did not reveal the pathogenic mutation of GAA gene but a DMD gene hemizygous variation (c.5571del, p. Lys1857AsnfsTer8), so he was diagnosed with DMD as well. Compared with the case 1, his GAA activity was not that low, and that was because his two GAA pseudo deficiency alleles were heterozygous, as it was showed in his GAA genetic analysis.
Conclusions: Pseudo deficiency alleles can cause remarkable reduction of GAA activity, like levels found in Pompe disease. When a patient with elevated creatine kinase and low GAA activity, the diagnosis should be carefully considered, genetic analysis is recommended.

关键字 acid α-glucosidase, pseudo deficiency alleles, Duchenne muscular dystrophy, creatine kinase
分类：20. Others 其它

1565

The economic burden of medical treatment of children with asthma in China

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Background: At present, there are few studies on the economic burden and medical treatment of children with asthma in China. Thus this study aimed to investigate the economic burden of medical treatment of children with asthma in China.
Method: The 2015 China Medical Insurance Research Association (CHIRA) database was searched for patients with asthma from 0 to 14 years old. A cross-sectional study with cost analysis was conducted.
Results: The annual per capita direct medical cost was RMB 525 (US$75) related to asthma. Totaling 58% of the medical expenditure for asthma was covered by insurance in China, the majority of which were direct medical costs. Those that have the highest rates of using antibiotics were central China (100.0%), children aged 3 years and under (63.6%), as well as fourth-tier and fifth-tier cities (77.1%). Outpatient clinics (98.58% vs 1.42%, $P < 0.01$), tertiary hospitals (62.08% vs 37.92%, $P < 0.01$), and general hospitals (72.27% vs 27.73%, $P < 0.01$) were more often visited than the inpatient clinics, secondary and primary as well as the specialized clinics, respectively.
Conclusion: The economic burden of childhood asthma in China is relatively low, and the national medical insurance reduces their economic burden to a large extent. Abuse of antibiotics in treating asthma was found in China. There remain opportunities to strengthen the hierarchical medical system, reducing hospitalization and emergency visits, and ultimately reducing the economic burden of children with asthma.

关键字 Childhood asthma, Economic burden, China medical insurance research association (CHIRA) database

Category: 20. Others 其它

1688

SYSTEMATIC REVIEW ON THE USEFULNESS AND APPLICABILITY OF DISTANCE LEARNING MODALITIES AMONG STUDENTS IN THE MEDICAL AND ALLIED HEALTH FIELDS IN THE TIME OF COVID-19

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Abstract Content To determine the distance learning modalities available during the COVID-19 pandemic time among students in the medical and allied health fields

Methods a. DESIGN: This is a systematic review wherein before a study is included, they were screened for their internal and external consistency, which is also provided by the Newcastle-Ottawa Quality Assessment Scale for Observational Studies
b. SETTING: The study setting scoped different places where distance learning modalities are available among students in the medical and allied health fields in the time of COVID-19
c. PARTICIPANTS: Students in the medical and allied health fields in time of COVID-19
d. MAIN OUTCOME MEASURE(S): Usefulness and applicability of distance learning modalities

Results Eleven studies were found from the database searches, and from these, six were included in the analysis. The population yielded very large heterogeneity (I2=67.10%), hence no statistically significant forest plots can be generated. Lectures conducted either synchronously or asynchronously using online learning management systems and platforms were the main modes of distance learning employed during this period. Outcomes among students have been generally favorable for continuing education, but issues and concerns were noted regarding their online connectivity and computer access which limited their learning experience

Conclusion Online learning is the predominant mode of distance learning employed at this time, and the perceptions of the students undergoing these curricula have been favorable thus far, with a few reporting issues related to their internet connectivity and computer access, which can hinder their progress with the completion of school requirements

Key words distance learning, health professions education, COVID-19
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