Evaluation of Medication Therapy Management service for children with epilepsy in clinic: A pilot randomized controlled trial

1. Introduction

In 2003, The United States Congress legislated "The Medicare Prescription Drug, Improvement, and Modernization Act (MMA)", which required insurance companies to provide Medication Therapy Management (MTM) services (MTMS) for beneficiaries enrolled in Medicare Part D, to optimize effects of treatments and reduce risks of adverse drug events (ADE) [1,2]. The MMA identified the following three key goals of MTMS: provision of education and counselling to improve enrollees' understanding of their medications, improvement of medication adherence, and detection of adverse drug reactions (ADR) and patterns of improper prescription medication use [3]. MTMS consists of five core elements, namely: medication therapy review (MTR), personal medication record (PMR), medication-related action plan (MAP), intervention and/or referral, documentation and follow-up, the sequence of which can be adjusted according to the needs of patients [4].

Compared with conventional pharmaceutical care, MTMS has obvious advantages and has significant clinical effects in the field of chronic diseases [5]. Chronic diseases in childhood, such as chronic kidney disease, asthma, and mental disorders, with the characteristics of long course (more than 3 months), repeated attacks and difficult to cure, will seriously interfere with the normal life of children [6]. Many studies have proposed the application of MTMS in the field of chronic diseases in childhood, but it developed slowly and the implementation effects is unclear currently.

Epilepsy is a chronic brain disease caused by a variety of causes, characterized by recurrent, paroxysmal and transient central nervous system dysfunction with excessive discharge of brain neurons [7]. The incidence of epilepsy in children is 3.9-5.1‰ in China, and the disability rate is as high as 25.0%-30.3%. Meanwhile, children with epilepsy have a 2 to 3 times higher risk of death than the general population. Repeated seizures of epilepsy also bring heavy burdens to individuals, families and society [7-10].

Inappropriate using of medicines was a serious threat to patients, which could result in a great waste of health resources [11]. At present, medication is the most important means of antiepilepsy in children, but the drug-related problems (DRPs) in aspects of effectiveness, safety and adherence are serious: (1) The complicated medication regimen of epilepsy is prone to the occurrence of DRPs [7]. (2) Due to the special physiological characteristics of children, long-term antiepileptic drugs will increase the risk of ADE, such as common liver dysfunction, nausea, rash, drowsiness, dizziness, abnormal blood cells, etc. (3) Children's poor medication adherence makes it impossible to guarantee the effectiveness of antiepileptic drugs: a systemic review showed that the medication adherence rate of children with epilepsy in China ranged from 33% to 88.1% and the result by Meta-analysis was 62% [8].

Therefore, the aim of this empirical study was to verify the effects of MTMS for children with epilepsy in clinic. At the same time, it can provide methodological reference for the application of MTMS among children with other chronic diseases.

2. **Methods**

2.1 Participants

The participants were children with epilepsy admitted to the clinic of West China Second Hospital of Sichuan University from August to November, 2019. Participants were enrolled according to the following criteria: Inclusion criteria: (1) The population were outpatients with epilepsy aged 0-18 years; (2) The diagnostic criteria conformed to the International League Against Epilepsy classification [12]; (3) The patients have been taking antiepileptic drugs and had epileptic seizures within three months; (4) The patients or their guardians were willing to fill in the questionnaires after they were given full informed consent. Exclusion criteria: (1) The patients suffered other non-drug-related serious complications; (2) The patients or their guardians were unable to communicate effectively with researchers, due to disturbance of consciousness, aphasia or deafness, etc; (3) The patients were lost or unable to follow up.

When a patient was enrolled, he/she would be allocated to a group randomly

according to a table of random numbers. We did not implement the blind method, because it would affect the children and their guardians' compliance seriously in the current health care environment.

3.2 Interventions

In experiment group, pharmacists cooperated with doctors to provide MTMS according the five core elements of MTMS [4].

- *MTR: Through electronic medical records and interviews with patients, the pharmacists collected the patients' medication-related information to conduct medication review. The pharmacists then assesses the medication regimens, the medication adherence, the medication belief, the level of disease awareness and so on to identify the presence of DRPs.*
- *PMR: The pharmacists carefully gathered participants' medication-related information for comprehensive personal medication record, including patients and their families' basic information, medication review and personal medication records, to enhance the continuity of care provided to patients and prepare for the next step of MTMS.*
- *MAP: The pharmacists provided individualized MAP of medication self-management for patients. The MAP included action steps, notes and medication education material for patients.*
- *Intervention and/or referral: The pharmacists discussed with doctors and provided interventions to solve identified DRPs; If there were some DRPs that couldn't be solved, the pharmacists referred patients to a doctor or other health care professional.*
- *Documentation and follow-up: The pharmacists documented the information of follow-up and interventions.*

In the control group, the pharmacists provided usual service (US), such as prescription reviews, drug dispensing and medication instructions in outpatient pharmacy.

3.3 Outcomes and measures

Medication adherence measured by the Morisky Medication Adherence Scale [13] was taken as the primary outcome. The scale consists of eight items, and the score ranges from 0 to 8 points (the higher score indicates greater adherence). The range of score was divided into 3 classifications (score<6, 6≤score <8, score=8), which were defined as poor, average and good adherence, respectively [14,15]. In addition, a

score of 6 to 8 was defined as qualified. Medication adherence was evaluated at the time of enrollment, intervention for 1 month, 2 months and 3 months, respectively.

Meanwhile, there were several secondary outcomes. Firstly, the effectiveness of antiepileptic drugs was measured by the number of seizures. Secondly, the safety of antiepileptic drugs was measured by frequency and causes of DRPs [15]. Thirdly, medication belief was measured by Beliefs about Medical Questionnaire [16], which includes two dimensions: beliefs about the necessity of medication and concerns about it [17]. Each dimension has 5 items, the score of which ranges from 1 to 5 (the higher score indicates greater belief). Fourthly, level of disease awareness was measured by the questionnaire designed by the researchers. The questionnaire contains 20 questions, the total score of which is 20, with 1 point for correct answers and no points for wrong answers. The range of score was divided into 3 classifications (score$\geqslant$16, 12$\leqslant$score < 16, and <12), which were defined as good, average and poor disease awareness, respectively. In addition, a score of 12 to 20 was defined as qualified. Finally, through telephone follow-up, the children and their guardians' degrees of satisfaction were surveyed by five-point Likert scale.

3.4 Data analysis

The proportion of good adherence was taken as the main outcome, so its difference test between the two groups was used to calculate the sample size (I error α= 0.05, II error β= 0.1) [18]. The calculation formula is as follows:

$$n_1 = k\, n_2$$

$$n_2 = (Z_{1-\alpha/2} + Z_{1-\beta})^2 [p_1(1-p_1)/k + p_2(1-p_2)] / (p_1-p_2)^2$$

(n_1： Sample size of control group, n_2： Sample size of experiment group, p_1： the proportion of good adherence in control group, p_2： the proportion of good adherence in experiment group, k： Rate of sample size in the two groups)

The superiority test of sample size was calculated with *P1* =62.1% and *P2* =96.3% [19], and the results showed 22 participants were needed for each group. Considering the loss of follow-up, the sample size was determined to be at least 30 for each group.

Microsoft Office Excel 2016 was used for data collection and SPSS 23.0 software was used for statistical analysis. Continuous variables were expressed as mean ± standard

deviation (SD) with use of t test. Categorical variables were expressed as percentage (%) with use of χ^2 test or Fisher test. The test level was $\alpha=0.05$, and $P<0.05$ was considered statistically significant.

3. Results

4.1 Baseline demographics of participants

In this study, 76 children with epilepsy were enrolled, 11 of them were lost to follow-up, and 65 of them completed the follow-up visits. Among them, 33 were allocated to the MTMS group, and 32 were allocated to control group. The analysis of baseline demographics showed that 56.92% (n=37) participants were males and the age of them ranged from 4 months to 14 years old. Most of them were uneducated (n=30, 46.15%) or in primary school (n=24, 36.92%). The children's families mainly lived in cities (n=50, 76.92%), and the total income monthly of the families mainly ranged from 5000 to 10000 yuan (n=23, 35.38%), and the medical expenses were mainly paid out of their own pocket (n=57, 87.69%). Only one child in the control group had a family history of epilepsy. The children's parents were mainly in high school or technical secondary school (n=22, 33.85%) and junior college (n=21, 32.31%). According to the analysis of baseline information, the differences of two groups were not statistically significant in all directions ($P>0.05$), as shown in Table 1.

4.2 Medication adherence

There was no significant difference in medication adherence between the two groups at baseline. The proportion of poor adherence (score<6) decreased significantly and the proportion of qualified adherence ($6 \leqslant$ score $\leqslant 8$) increased significantly throughout the MTMS. On the contrary, the proportion of poor and qualified adherence had no significant change in the US group (See Table 2 for details). And the scores of medication adherence of MTMS group showed an overall upward trend, which were: 6.45±0.90 at baseline, 6.73±0.76 after 1 month, 6.97±0.48 after 2 months, and 7.36±0.48 after 3 months. The scores of medication adherence of the US group

showed a fluctuating up and down trend, which were: 6.47 ± 1.34 at baseline, 6.53 ± 1.24 after 1 month, 6.21 ± 1.25 after 2 months, and 6.31 ± 1.16 after 3 months.(See Table 3 for details)

4.3 Effectiveness of antiepileptic drugs

There was no statistical difference in the number of seizures per month between the MTMS group and the US group before and after the intervention (P>0.05), as shown in Table 4.

4.4 Safety of antiepileptic drugs

During the intervention and follow-up, 92 DRPs were identified in the MTMS group, and 83 of them were resolved. The main causes of DRPs were ADEs reported by the children or their guardians (n=39, 42.39%) and medication adherence problems (n=33, 35.87%). Among them, the ADEs included drowsiness (n=20), absent-minded (n=8), dysphoria (n=5), and so on. Medication adherence problems included taking medicines at inappropriate time (n=17), forgetting to take medicines (n=8), taking medicines at inappropriate frequency (n=5), and taking more/less medicines than prescribed (n=3). Nine DRPs were unsolved, because the intervention was ineffective or the children's guardians did not accept the intervention.

In US group, 63 DRPs were identified, and 15 of them were resolved. The main causes of DRPs were ADEs reported by the children or their guardians (n=27, 42.86%) and medication adherence problems (n=22, 34.92%). Among them, the ADEs included drowsiness (n=14), dysphoria (n=6), absent-minded (n=5), and so on. Medication adherence problems included forgetting to take medicine (n=11), taking medicine at inappropriate time (n=5), taking medicine as inappropriate frequency (n=3), taking more/less medicine than prescribed (n=2), and stopping taking medicine without permission (n=1).

4.5 Medication behavior

4.5.1 Medication belief

There was no significant difference in medication belief between the two groups at baseline (P>0.05). After the intervention, the scores of necessity dimension in the MTMS group were higher than those in the US group, and the scores of concern

dimension were lower than those in the US group, with statistically significant differences. In the MTMS group, the overall trend of scores in necessity dimension was on the rise, while the overall trend of scores in necessity dimension was downward. The former was higher than the latter, making the results of medication belief were positive. In the US group, the overall scores in necessity dimension was slightly lower, while the overall trend of scores in necessity dimension bounced up and down. The former was higher than the latter, making the results of medication belief were negative (See Table 6 for details).

4.5.2 Level of disease awareness

At baseline, the level of disease awareness among children's guardians in MTMS group and the US group all reached qualified standard and there was no statistical difference in the score ($P>0.05$). After the intervention, the number of good disease awareness and the score of disease awareness among guardians in the MTMS group were higher than those in the US group, and the differences were statistically significant ($P<0.05$) (See Table 7 and Table 8 for details).

4.5.3 Degrees of satisfaction

At baseline, the degrees of satisfaction in the MTMS group was "satisfied" or "very satisfied", while they were "general", "satisfied" or "very satisfied" in the US group. After the intervention, the degrees of satisfaction in the MTMS group and the US group were both "satisfied" or "very satisfied". During the whole intervention process except enrollment, the degrees of satisfaction in MTMS group was higher than those in the US group, and the difference was statistically significant ($P<0.05$) (See Table 9 for details).

4. Discussion

4.1 Comparison between MTMS and usual pharmaceutical service

In MTMS, pharmacists focus on children and cooperate with doctors to intervene in the whole process of treatment. In particular, MTMS plays an important role in improving medication adherence, improving effectiveness and safety of treatment. Frequent communications among pharmacists, doctors and patients are required

throughout the process of intervention, from the assessment of drug-related needs to the identification of DRPs, from the determination of treatment goals to the formulation of care plans, and the follow-up to evaluate actual treatment outcomes.

In usual pharmaceutical service, pharmacists focus on prescriptions, and complete the following interventions independently in outpatient pharmacy: (1) Prescription reviews: the type of seizures usually isn't noted in prescriptions, so prescription reviews don't involve rationality of antiepileptic drug selection, dosage and treatment duration of different treatment stages, and ADRs. (2) Drug dispensing: Pharmacists dispense prescription drugs accurately according to the operating procedures. (3) Medication instructions: Because of the large workload of distribution, pharmacists only inform patients of medication instructions briefly. Generally, it won't involve the monitoring of major ADRs, precautions of lifestyle or diet, follow-up time and so on.

4.2 The clinical effects of MTMS needs further verification

MTMS aims at managing the medications in patients with chronic diseases, which provides education and guidance for patients, and identifies and solves DRPs timely in the whole process of treatment. The ultimate goal is gradually achieve patients' self-management of chronic diseases from adherence, living habits, physical and mental health, etc. In this study, except that there was no significant difference in effectiveness between the two groups before and after intervention, other results showed that the effects of the MTMS group were better than those of the US group after intervention with statistically significant differences. The possible reasons why the effectiveness wasn't improved are as follows: (1) The types of epilepsy are various, and the seizures of epilepsy are complex and even easy to repeat. Even if patients' medication adherence is good, it's still possible that the effectiveness can't be improved. (2) Studies showed that successful treatment of epilepsy generally requires taking medicines for 2-5 years [10], and the follow-up time in this study is short, so the effectiveness may not be observed. (3) There are individual differences in the effectiveness of treatment among children with epilepsy. However, the sample size of this study is small, which may lack sufficient data to prove the effectiveness of antiepileptic drugs.

At present, it remains controversial whether MTMS can ultimately improve patients' clinical outcomes in many foreign studies. In 2015, Meera Viswanathan et al. conducted a systematic review that aimed to evaluate the clinical outcomes of MTMS, and the results found that MTMS might reduce the frequency of DRPs (including non-adherence) and reduce the usages and costs of some health care, but the improvement of clinical health outcomes still needed more evidence [20].

4.3 Limitations of this study

The sample size in this randomized controlled study was small and the follow-up time was short. The feasibility, effectiveness and generalizability of the MTMS still need to expand the sample size for further verification. This study lacks an evaluation of the economy of MTMS.

5. Conclusion

Taking West China Second Hospital of Sichuan University as an example, we studied the application of MTMS for children with epilepsy in clinic, which proved MTMS could improve medication adherence, safety and medication behavior. At the same time, the results of this study provided methodological reference for the application of MTMS among children with other chronic diseases.

Table 1 Baseline demographics and univariate analysis of participants

Attribute	Classification	MTMS group（n=33）	US group（n=32）	All participants	p-Value
Year	≤28 days	0	0	0	1.997, 0.674
	28 days<y≤1year	4	3	7	
	1 year<y≤3 years	13	16	29	
	3 years<y≤6 years	10	7	17	
	6 years<y≤12 years	6	5	11	
	12 years<y≤18 years	0	1	1	
Gender	Male	20	17	37	0.371, 0.543
	Female	13	15	28	
Education	Uneducated	16	14	30	3.858, 0.397
	Kindergarten	3	5	8	
	Primary school	14	10	24	
	Junior high school	0	2	2	
	Senior high school	0	0	0	
	Others (Pre-school)	0	1	1	
Residence	Urban resident	29	21	50	3.365, 0.067
	Rural resident	4	11	15	
Total income per month (yuan)	0-3000	3	5	8	1.055, 0.821
	3001-5000	9	7	16	
	5001-10000	11	12	23	
	⩾10001	10	8	18	
payment method of medical expenses	Self-paying	29	28	57	1.134, 1.000
	Medical insurance	3	4	7	
	Free medical care	0	0	0	
	Commercial insurance	1	0	1	
Family history	Yes	0	1	1	1.047, 0.492
	No	33	31	64	
Father's	Primary School or Below	0	1	1	2.458,

(mother's) education	Junior high school	2	4	6	0.678
	High school or technical secondary school	13	9	22	
	Junior college	10	11	21	
	Bachelor or above	8	7	15	

Table 2 Classifications of medication adherence of children with epilepsy in the MTMS group vs. the US group

Group	Classification				χ^2, P-value
	Poor [0, 6)	Average [6, 8)	Good [8]	Qualified [6, 8]	
At baseline					
MTMS group (n=33)	7	23	3	26	3.022, 0.216
US group (n=32)	9	16	7	23	
After 1 month					
MTMS group (n=33)	3	28	2	30	3.374, 0.180
US group (n=32)	5	21	6	27	
After 2 months					
MTMS group (n=33)	0	31	2	33	**15.174, 0.000**
US group (n=32)	10	18	4	22	
After 3 months					
MTMS group (n=33)	0	23	10	33	**10.541, 0.005**
US group (n=32)	8	19	5	24	

Table 3 Scores of medication adherence of children with epilepsy in the MTMS group vs. the US group

Group	Score					t, P-value
	Poor [0, 6)	Average [6, 8)	Good [8]	Qualified [6, 8]	Total [0, 8]	
At baseline						
MTMS group (n=33)	5.29±0.64	6.61±0.52	8.00±0.00	6.77±0.67	6.45±0.90	-0.341, 0.734
US group (n=32)	4.72±1.09	6.72±0.55	8.00±0.00	7.11±0.76	6.47±1.34	

After 1 month						
MTMS group (n=33)	5.17±0.80	6.81±0.48	8.00±0.00	6.89±0.56	6.73±0.76	0.470, 0.640
US group (n=32)	4.25±0.85	6.65±0.53	8.00±0.00	6.95±0.74	6.53±1.24	
After 2 months						
MTMS group (n=33)	0.00±0.00	6.90±0.41	8.00±0.00	6.97±0.48	6.97±0.48	**3.048, 0.003**
US group (n=32)	4.72±0.84	6.64±0.46	8.00±0.00	6.89±0.68	6.21±1.25	
After 3 months						
MTMS group (n=33)	0.00±0.00	7.08±0.24	8.00±0.00	7.36±0.48	7.36±0.48	**4.619, <0.001**
US group (n=32)	4.72±0.59	6.54±0.47	8.00±0.00	6.84±0.73	6.31±1.16	

Table 4 The number of seizures per month of children with epilepsy in the MTMS group vs. the US group

Group	The number of seizures per month				χ^2, P
	[0-5]	(5-15]	(15, 20]	>20	
At baseline					
MTMS group (n=33)	22	5	4	2	3.284, 0.336
US group (n=32)	27	3	2	0	
After 1 month					
MTMS group (n=33)	23	5	5	0	2.028, 0.398
US group (n=32)	27	3	2	0	
After 2 months					
MTMS group (n=33)	21	6	5	1	1.468, 0.840
US group (n=32)	26	4	2	0	
After 3 months					
MTMS group (n=33)	23	5	4	1	3.043, 0.364
US group (n=32)	27	4	1	0	

Table 5 The DRPs of children with epilepsy in the MTMS group vs. the US group

DRPs	Details	Interventions	Accepted interventions and resolved DRPs
MTMS group (n=92)			
ADEs reported by the children or their guardians (n=39)	Drowsiness (n=20)	① Informing the children or their guardians of the common ADRs of antiepileptic drugs; ② Reporting ADEs to doctors in time; ③ Reformulating the medication regimen; ④ Recommending to visit doctors again for examination	n=18
	Absent-minded (n=8)		n=8
	Dysphoria (n=5)		n=5
	Anorexia (n=3)		n=2
	Rash (n=2)		n=2
	Dizziness (n=1)		n=1
Medication adherence problems (n=33)	Taking medicines at inappropriate time (n=17)	① Providing medication education, informing the children or their guardians of the importance of medication adherence in the treatment of epilepsy; ② Providing regular follow-ups and telephone reminders	n=17
	Forgetting to take medicines (n=8)		n=7
	Taking medicines at inappropriate frequency (n=5)		n=5
	Taking more/less medicines than prescribed (n=3)		n=3
Treatment duration (n=8)	Duration of treatment too long (n=8)	① Discussing with doctors and reformulating the duration of treatment; ② Providing education and recommending to visit doctors regularly	n=8
Unreasonable drug selection (n=5)	Off-label use (n=4)	① Discussing with doctors and re-selecting alternative drugs; ② Discussing with doctors and reformulating the medication regimen	n=1
	Inappropriate drug form (n=1)		n=1
No inappropriate outcome monitoring (n=4)	No inappropriate outcome monitoring (n=4)	① Discussing with patients' doctors and reformulating the medication regimen; ② Discussing with patients' doctors and carrying out relevant outcome monitoring	n=2
No indication for drug (n=3)	No indication for drug (n=3)	① Discussing with patients' doctors and clarifying the diagnosis in medical history	n=3
US group (n=63)			

Adverse events reported by the children's guardians (n=27)	Drowsiness (n=14)		n=5
	Absent-minded (n=5)		n=1
	Dysphoria (n=6)		n=2
	Rash (n=1)		n=1
	Diarrhea (n=1)		n=1
Medication adherence problems (n=22)	Forgetting to take medicines (n=11)	Pharmacists and doctors provided routine medical services, except when the children or their guardians reported or asked for solutions	n=4
	Taking medicines at inappropriate time (n=5)		n=0
	Taking medicines at inappropriate frequency (n=3)		n=0
	Taking more/less medicines than prescribed (n=2)		n=0
	Stopping taking medicines without permission (n=1)		n=1
No inappropriate outcome monitoring (n=6)	No inappropriate outcome monitoring (n=6)		n=0
Treatment duration (n=3)	Duration of treatment too long (n=3)		n=0
Unreasonable drug selection (n=3)	Unreasonable drug selection (n=3)		n=0
No indication for drug (n=2)	No indication for drug (n=2)		n=0

Table 6 Scores of medication belief of children with epilepsy in the MTMS group vs. the US group

Group	Score			
	Necessity dimension	*t*，P-value	Concern dimension	*t*，P-value
At baseline				
MTMS group (n=33)	3.60±0.56	0.633，0.344	3.45±0.71	1.015，0.314
US group (n=32)	3.46±0.60		3.29±0.56	
After 1 month				
MTMS group (n=33)	3.88±0.56	**3.340，0.001**	3.38±0.71	-0.483，0.631
US group (n=32)	3.44±0.52		3.46±0.64	
After 2 months				
MTMS group (n=33)	4.11±0.43	**6.624，＜0.001**	3.21±0.68	-0.674，0.503
US group (n=32)	3.31±0.54		3.32±0.59	
After 3 months				
MTMS group (n=33)	4.29±0.47	**8.237，＜0.001**	3.19±0.58	**-2.553，0.013**
US group (n=32)	3.32±0.48		3.57±0.62	

Table 7 Level of disease awareness of children' guardians in the MTMS group vs. the US group

Group	Classification				χ^2, P-value
	Poor (<12)	Average [12, 16)	Good (≥16)	Qualified (≥12)	
At baseline					
MTMS group (n=33)	0	14	19	33	2.625, 0.138
US group (n=32)	0	20	12	32	
After 1 month					
MTMS group (n=33)	0	5	28	33	**5.265, 0.028**
US group (n=32)	0	13	19	32	
After 2 months					
MTMS group (n=33)	0	3	30	33	**14.788, <0.001**
US group (n=32)	0	17	15	32	

After 3 months					
MTMS group (n=33)	0	0	33	33	**21.888, <0.001**
US group (n=32)	0	16	16	32	

Table 8 Scores of disease awareness of children's guardians in the MTMS group vs. the US group

Group	Score					*t*, P
	Poor (<12)	**Medium [12-16)**	**Good [16, 20]**	**Qualified [12, 20]**	**Total [0, 20]**	
At baseline						
MTMS group (n=33)	0.00±0.00	14.21±0.70	16.74±0.81	15.67±1.47	15.67±1.47	1.793, 0.078
US group (n=32)	0.00±0.00	13.8±1.15	16.83±0.72	14.94±1.79	14.94±1.79	
After 1 month						
MTMS group (n=33)	0.00±0.00	14.00±1.00	17.04±0.88	16.58±1.41	16.58±1.41	**3.412, 0.001**
US group (n=32)	0.00±0.00	14.23±1.01	16.26±0.56	15.44±1.27	15.44±1.27	
After 2 months						
MTMS group (n=33)	0.00±0.00	14.33±1.15	17.17±0.87	16.91±1.21	16.91±1.21	**5.943 , ＜0.001**
US group (n=32)	0.00±0.00	14.12±0.60	16.27±0.46	15.12±1.21	15.12±1.21	
After 3 months						
MTMS group (n=33)	0.00±0.00	0.00±0.00	18.00±1.27	18.00±1.27	18.00±1.27	**9.107 , ＜0.001**
US group (n=32)	0.00±0.00	14.19±0.66	16.27±0.46	15.22±1.18	15.22±1.18	

Table 9 Degrees of satisfaction of children' guardians in the MTMS group vs. the US group

Group	Score					χ^2, P
	Very dissatisfied (1)	**Dissatisfied (2)**	**Medium (3)**	**Satisfied (4)**	**Very satisfied (5)**	
At baseline						
MTMS group (n=33)	0	0	0	15	18	4.156，0.08

US group (n=32)	0	0	1	21	10	
After 1 month						
MTMS group (n=33)	0	0	0	6	27	**11.823，0.001**
US group (n=32)	0	0	1	18	13	
After 2 months						
MTMS group (n=33)	0	0	0	6	27	**15.326，＜0.001**
US group (n=32)	0	0	1	20	11	
After 3 months						
MTMS group (n=33)	0	0	0	6	27	**16.942，＜0.001**
US group (n=32)	0	0	0	22	10	

Reference

[1] Mao L, Zhe C, Linan Z, et al. Analysis of Medication Therapy Management at Home and Abroad [J]. China Pharmacy,2019(17):2305-2310.

[2] Mcgivney MS, Meyer SM, Duncan-Hewitt W, et al. Medication therapy management： its relationship to patient counseling, disease managemen, and pharmaceutical care [J]. J Am Pharm Assoc, 2007, 47(5):620-628.

[3] The Medicare Prescription Drug, Improvement, and Modernization Act, HR 1/ Pub. L. No. 108-173, 2003 Dec 8 [online]. Available from URL: http://www.cms.hhs.gov/MMAUp date/down loads/PL108-173summary.pdf

[4] American Pharmacists Association and National Association of Chain Drug Stores Foundation. Medication therapy management in pharmacy practice: core elements of an MTM service model (version 2.0) [J]. J Am Pharm Assoc, 2008; 48 (3): 341-353.

[5] Viswanathan M, Kahwati LC, Golin CE, et al. Medication therapy management interventions in outpatient settings: a systematic review and meta-analysis [J]. JAMA Intern Med, 2015,175(1):76-87.

[6] Mokkink LB, van der Lee JH, Grootenhuis MA, et al; Dutch National Consensus Committee Chronic Diseases and Health Conditions in Childhood. Defining chronic diseases and health conditions in childhood (0-18 years of age): national consensus in

the Netherlands [J]. Eur J Pediatr,2008,167(12):1441-1447.

[7] China Association Against Epilepsy. Clinical practice guidelines: Epilepsy Section [J]. 2015.

[8] Chunsong Y, Hongyi S, Lingli Z, et al. Study on Current Status and Influencing Factors of Medication Compliance in Children With Epilepsy in China [J]. Chinese Pharmaceutical Affairs,2017,31(12):151-159.

[9] Lin C, Xiaoshan W. Progress in epidemiological investigation of epilepsy in China [J]. Journal of International Neurology and Neurosurgery,2012,39(2):161-164.

[10] Xiaoguang S, Ronghua C, Jingyun D, et al. An Epidemiological Investigation on Epilepsy Among Children of 0-14 Age in Jiangsu Province [J]. Journal of Nanjing Medical College,1992(2):170-172.

[11] Song J, Zhang L, Li Y, et al. Indicators for assessing quality of drug use: A systematic literature review [J]. J Evid Based Med,2017,10(3):222-232.

[12] Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009 [J]. Epilepsia,2010,51:676 –685.

[13] Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence [J]. Med Care,1986,24(1):67-74.

[14] Morisky D E, Green L W, Levine D M. Concurrent and Predictive Validity of a Self-reported Measure of Medication Adherence [J]. Medical Care,1986,24(1):67-74.

[15] Lili M, Xiaodong G, Xiaoxiong X, et al. Review of Compliance Assessment Methods [J]. Chinese Pharmaceutical Affairs,2016,30(4):388-393.

[16] Horne R, Weinman J, Hankins M. The Beliefs about Medicines Questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication [J]. Psychol Health,1999,14:1-24.

[17] Yang L, Zheng L, Meiying H, et al. Beliefs about antidepressants among Chinese elderly people with depressive disorder [J]. Chin J Nurs,2015,50(5):518-521.

[18] Gregory S, Karl K, Travis G, et al. Implementation of a medication therapy management collaborative within a pediatric health system [J]. J Am Pharm Assoc, 2018:S1544319118301948.

[19] Tang F, Zhu G, Jiao Z, et al. The effects of medication education and behavioral intervention on Chinese patients with epilepsy [J]. Epilepsy and Behavior, 2014,37:157-164.

[20] Viswanathan M, Kahwati L C, Golin C E, et al. Medication Therapy Management Interventions in Outpatient Settings A Systematic Review and Meta-analysis[J]. JAMA Internal Medicine,2014,175(1):76-87.