Clinical pharmacist-led educational tool effect on pediatric patients with epilepsy in Jordan

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Abstract

Aim: To investigate the effect of a clinical pharmacist-led educational tool on pediatric patients with epilepsy in Jordan. Specifically on the efficacy, safety, adherence to antiepileptic drugs (AEDs), satisfaction with information about AEDs provided to the caregivers, and quality of life (QoL). Methods: This was a randomized controlled trial where pediatric patients were randomly assigned to the intervention (n=41) or the control (n=40) group. 30-minute clinical pharmacist-led educational interview to the parent/caregiver was provided to the intervention group as add-on to standard medical care received by the control group. Efficacy was measured by number of seizure-free patients, while epilepsy specific questionnaires were used to evaluate safety, adherence, satisfaction with information about AEDs and QoL; measured at baseline and after 8-week follow-up. Results: The intervention group had 63.9% seizure free patients at follow up vs. 31.7% at baseline (P-value <0.001), and the control group had 48.6% at follow up vs. 27.5% at baseline (P-value <0.05); with no significant difference between groups (P-value > 0.05). At follow-up, mean pediatric epilepsy side effects questionnaire (PESQ) score was reduced in the intervention group (P-value <0.001), and increased in the control group (P-value <0.001); with no significant difference between groups (P-value=0.08). While the intervention group had a significant higher mean score of adherence (P-value <0.0001), and higher satisfaction with information (P-value <0.0001), and a higher QoL (P-value <0.05). There was a significant positive correlation between satisfaction and adherence (r=0.682, P-value < 0.0001), satisfaction and QoL (r=0.298, P-value < 0.05), adherence and QoL (r=0.323, P-value < 0.01). While, satisfaction and safety, safety and QoL correlated significantly and negatively (r=-0.263, P-value < 0.05 and r=-0.782, P-value < 0.0001, respectively) Conclusion: Clinical pharmacist-led educational tool had a positive outcome on pediatric patients with epilepsy with regard to efficacy, safety, adherence, satisfaction with information about AEDs and QoL.

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DISCLOSURE

The authors declare no conflict of interest

Running Title: Clinical pharmacist, pediatrics, epilepsy

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Results: The intervention group had 63.9% seizure free patients at follow up vs. 31.7% at baseline (P -value <0.001), and the control group had 48.6% at follow up vs. 27.5% at baseline (P -value <0.05); with no significant difference between groups (P - value > 0.05). At follow-up, mean pediatric epilepsy side effects questionnaire (PESQ) score was reduced in the intervention group (P -value <0.001), and increased in the control group (P -value <0.001); with no significant difference between groups (P -value=0.08). While the intervention group had a significant higher mean score of adherence (P- value <0.0001), and higher satisfaction with information (P -value <0.0001), and a higher QoL (P -value <0.05). There was a significant positive correlation between satisfaction and adherence (r=0.682, P -value < 0.0001) , satisfaction and QoL (r=0.298, P -value < 0.05), adherence and QoL (r=0.323, P -value < 0.01). While, satisfaction and safety, safety and QoL correlated significantly and negatively (r=-0.263, P -value < 0.05 and r=-0.782, P -value < 0.0001, respectively)

Conclusion: Clinical pharmacist-led educational tool had a positive outcome on pediatric patients with epilepsy with regard to efficacy, safety, adherence, satisfaction with information about AEDs and QoL.

Keywords: clinical-pharmacist, pediatrics, epilepsy

What's known?

- Including pharmacists in patients' routine care in hospital settings increased in the last few years worldwide.

- Acquiring an appropriate amount of knowledge about medication regimen and an adequate information regarding treatment are major reasons for improved patient outcomes.

What's new?

- Clinical pharmacist-led educational tool had a positive outcome on pediatric patients with epilepsy with regard to efficacy, safety, adherence, satisfaction with information about AEDs and QoL.

- Clinical pharmacist plays a pivotal role in the care of pediatric patients with epilepsy and thus should be included in the healthcare team for these patients.

1. INTRODUCTION

Epilepsy is a chronic neurological condition that affects people worldwide, in Arab countries, epilepsy is two-fold higher in children and young adults than in older adults (1), and the incidence and prevalence of epilepsy in children is higher in underdeveloped countries (2). Adverse drug reactions (ADRs) experienced from antiepileptic drugs (AEDs) can cause treatment withdrawal in up to 25% of cases, which will eventually lead to treatment failure (3), therefore, adherence should be strongly encouraged. In children, the rate of non-adherence to AEDs was 33%, and the main reasons for non-adherence were older age, or being diagnosed with generalized epilepsy rather than focal epilepsy, also parents' depressed mood was associated with non-adherence (4). Another study conducted in Saudi Arabia found that 38.3% of adolescents were non-adherent to their AEDs; factors affecting that were the age of the mother, number of family members, the number of administered AEDs, family's support, parents' relationship and the relationship between the patients and the healthcare provider (5).

Acquiring an appropriate amount of knowledge about medication regimen and an adequate information regarding treatment are major reasons for increased adherence to medications in patients with chronic diseases (6). Clinical pharmacists are an important part of the health care team, and engaging them in the management of patients has proved to increase efficacy and safety of treatment regimens (7). Pharmacist involvement in the patient education and counseling range from providing information about medications at the time of dispensing, to interventional counseling and drug monitoring throughout the period of treatment, and patients' self-management support. So, education and counseling provided by pharmacists was conducted for patients with different chronic diseases including epilepsy (8-15).

To date, only few studies have investigated the effect of clinical pharmacist conducted education on the efficacy and safety of AEDs in pediatric population, therefore, the aim of this study is to investigate the effect of a clinical pharmacist-led educational tool on the efficacy and safety of AEDs in pediatric patients with epilepsy in Jordan. In addition, we aimed to evaluate the satisfaction with the information about AEDs provided to the caregivers, and quality of life (QoL) in pediatric patients with epilepsy as well as the possible correlation between these parameters.

2. METHODS

2.1 Patients and study design

This study is a randomized, controlled, study with pre-test and post-test design to examine the efficacy of clinical pharmacist-led education on pediatric patients with epilepsy. It was conducted in two large hospitals in Jordan, over a period of six months from June 2020 to November 2020. Follow up was done eight-week after enrolment. The study was approved by the Institutional Review Boards (IRB) at both hospitals (No.80/2020/1007). Sample size was determined as 35 patients in each group based on effect size = 0.68 for difference in adherence as one of the endpoints measured (16), power = 80% and alpha = 0.05 were determined for this study.

Inclusion criteria were pediatric patients aged < 18 years old, with physician diagnosis of epilepsy and treated with AEDs. And the exclusion criteria were the presence of a neurological congenital disease or comorbid neurodevelopmental disability. Since the patients did not reach the legal age to consent for participation in the study, parent or caregiver written consent and patient verbal assent was taken if age is applicable after the aims and voluntary participation in the study was explained. No compensation was offered to patients or families.

Out of 1393 patients evaluated for suitability, 81 patients were enrolled in the study. Patients enrolled were randomly assigned into either the control or intervention group. Randomization was done using Research Randomizer® and allocation sequence was not shared with participants (Concealed). Follow-up was done after eight weeks (Figure 1).

2.2 Questionnaires

These epilepsy specific questionnaires were used to evaluate safety of AEDs, adherence to AEDs, satisfaction with information about AEDs and QoL in pediatric patients with epilepsy, they were answered by

the parent/caregiver twice at baseline and at follow-up, and it took from 15-20 minutes to answer these questionnaires:

1- Pediatric Epilepsy Side Effects Questionnaire (PESQ), which is a 19-item measure consisting of five subscales (cognitive, motor, behavioural, general neurological and weight) side effects, five-point Likert scale from one (Not Present) to five (High Severity) was used, finally, a score from 0-100 was calculated and a higher score indicates higher number and severity of side effects (17).

2- The 8-item Morisky Medication Adherence Scale (MMAS-8), it consists of eight questions with a score of zero or one, higher score means increased adherence (18), the validated Arabic version was used (19).

3- The Satisfaction with Information about Medicines Scale (SIMS), a 17-questions used to indicate whether the patients have received enough information about their prescribed medicines, it identifies patients' satisfaction with information about the action and usage of medication, and the potential problems of medication, a score of one or zero is given to each question, higher score indicate higher degree of satisfaction (20).

4- Pediatric Quality of Life Inventory (Peds QL) epilepsy module, it is used to assess quality of life in pediatric patients with epilepsy, and consists of five dimensions (Impact, Cognitive Functioning, Sleep/Rest, Executive Functioning, and Mood/Behavior). Five-point Likert scale from zero (Never) to four (Almost always) is used and a score out of 100 is given and higher score indicates lower problems. Use was authorized by Mapi Research Trust (21).

2.3 Intervention

The control group received the standard medical care, and the intervention group were provided an add-on 30-minute verbal face-to-face clinical pharmacist-led educational interview to the parent/caregiver. He/she was educated about his/her child medications and disease individually in an interactive manner.

The education material was reviewed by pediatric neurologists in both hospitals and flash cards were designed in Arabic for the disease education and for each AED separately to facilitate education. The educational session covered the following topics:

1- Education about epilepsy disease (signs and symptoms).

2-Antiepileptic drugs therapy education (treatment importance, benefits, importance of medication adherence, and treatment length).

3- Medication administration (dosing, when and how to take a dose, how to store the medication, and what to do in case of a missed dose).

4- Drug–drug or drug–food interactions.

5- Side effects of medications and what to do when experiencing side effects.

For equality reasons, the educational session was done after the end of the study for the control group.

2.4 Outcome measures

Outcomes of this study were the efficacy, safety and adherence to AEDs, satisfaction with information about AEDs and QoL in pediatric patients with epilepsy. Efficacy was particularly measured by comparing the number of pediatric patients who became seizure free during the study period. Comparison between the number of pediatric patients who are seizure free at baseline and who became seizure free at follow-up was done in each group separately, and comparing the number of seizure free patients between groups at baseline and follow up. Safety of AEDs was measured by the PESQ score, adherence to AEDs was measured by the 8-MMAS score, parent/caregiver satisfaction with information about AEDs was measured by the SIMS score, and finally, QoL in pediatric patients with epilepsy was measured by the PedsQL epilepsy module score. A comparison between the mean scores at baseline and at follow-up in each group, and comparing the means between groups at baseline and follow-up was done.

2.5 Statistical analysis

Data were coded, entered and analysed using the Statistical Package for Social Sciences (SPSS, version 24.0). All statistical tests were two-sided, and P values of <0.05 were considered statistically significant. Baseline demographics and clinical characteristics of patients were compared using Chi square test for categorical variables, and independent sample t-test for continuous variables. When comparing continuous variables within research groups in the same study arm, between baseline and end of the study, paired sample t-test was used. For categorical variables, McNemar test was used to compare the results within the same arm of study pre- and post-intervention. And when comparing the continuous variables between the different arms of the study, at baseline or at follow-up, independent sample t-test was used, for comparing the categorical variables Chi square test was used. Pearson correlation test was used to find correlations between continuous data.

3. RESULTS

3.1 Patients

81 patients were enrolled into either the control (n=40) or the intervention group (n=41). After 8 weeks, five (n=5, 12%) from the intervention group and five (n=5, 12.5%) from the control group were lost to follow up, due to inability to contact them by the phone numbers provided. Therefore, total number of patients included in the statistical analysis at follow up were 71 (87.65%), of them 36 (88%) in the intervention group and 35 (87.5%) in the control group (Figure 2). Table 1 shows the baseline demographic and clinical characteristics of the 81 patients.

The mean age of patients (±SD) in the intervention group was 8.63 ± 3.99 years, and in the control group was 8.9 ± 3.5 years. The highest percentage of pediatric epilepsy patients was in the age of 7-12 years (n=37) 45.7%, while patients aged 0-6 years were 33.3% (n=27), and the least percentage of patients was in the age of 13-18 years (n=17) 21%.

3.2 Outcomes

Patients were categorized into six categories according to the frequency of seizures in the previous six months prior to enrolment: 1- no seizures 2- one to two seizures 3- three to five seizures 4- one or more seizures per month 5- one or more seizures per week and 6- one or more seizures per day. At follow-up, there was inability to classify patients in category three (three to five seizures) as the follow up period was two months and three to five seizures would classify the patient in category four (one or more seizure per month).

Efficacy of AEDs was measured by comparing the number of patients who became seizure free after eight weeks of enrolment. Both groups had a significant increase in the number of patients who became seizure free at follow up compared to baseline (Figure 3). The intervention group had 23 (63.9%) seizure free patients at follow up vs. 13 (31.7%) at baseline (P -value <0.001), and the control group had 17 (48.6%) at follow up vs. 11 (27.5%) at baseline (P -value <0.05). The difference at follow-up, however, was not statistically significant between groups (P - value > 0.05). Table 2 shows the results of study outcomes. Safety of AEDs, adherence to AEDs, satisfaction with information about AEDs and patients QoL were measured using the mean scores of PESQ, MMAS-8, SIMS and PedsQL epilepsy module, respectively (Figure 4). Mean PESQ was reduced in the intervention group from 21.08 ± 10.59 to 18.91 ± 9.44 (P -value <0.001), and increased in the control group from 21.42 ± 12.16 to 23.73 ± 13.24 (P -value <0.001); with no significant difference between the study groups at follow-up (P -value=0.08). At follow-up, the intervention group had a significant higher mean score of adherence of 7.6 ± 0.9 vs. 5.8 ± 1.4 in the control group (P- value <0.0001), besides that, patients categorized with high level of adherence were significantly increased in the intervention group (Figure 5). And higher satisfaction with information about AEDs in the intervention group of 12.58 ± 1.4 vs. 2.7 ± 2.68 in the control group at follow-up (P -value <0.0001), as well as higher QoL of 75.09 ± 14.87 vs. 64.6 ± 21.58 in the control group (P -value <0.05). Correlation test was also done to investigate the association between the study outcomes (Table 3), and between the study outcomes and patients' demographic and clinical characteristics (Table 4).

4 DISCUSSION

This controlled interventional study aimed at assessing the impact of clinical pharmacist-led educational tool on pediatric patients with epilepsy in Jordan. Other studies should be done to have a more reliable, applicable and generalized findings. This study signifies the benefits from including the clinical pharmacist in the routine care of pediatric patients with chronic diseases including epilepsy. Improvements were also seen in the control group, and this underlines the importance of control group. Reasons for these improvements might be from the continued treatment at the specialized neurology clinics, and enthusiasm or motivation due to the baseline and follow up assessment done by the clinical pharmacist.

4.1 Efficacy

Previous studies on education effect on efficacy measured by the number of seizure free patients showed controversial results. Ibinda *et al.* (2014) had similar findings to ours, but education was provided by a nurse or clinical officer, it was found that there was no significant difference in number of seizure free patients between the intervention and the control groups, (50.8% vs. 46.8%), even after a follow up period of one year, a longer follow-up time than ours (22). Moreover, Tang *et al* . (2014) studied the effect of education by pharmacist in 59 patients with epilepsy. It showed a significant improvement in seizure control after a follow up period of six months, as the percentage of seizure free patients were increased from 5.7% to 50.9%, but it lacked a control group (i.e. with no education), thus, results from this study should be interpreted with caution (9). On the other hand, the effect of an educational program called MOSES showed significant improvement in seizure frequency in the intervention group compared to the control group over a period of six months, 19% improved in the intervention group vs. 7.2% in the control (P -value 0.04) (23).

As we provided education to all patients receiving AEDs regardless of their type, we did not perform a blood sampling for TDM as a measure of treatment efficacy as in Ma *et al* . (2019) study because not all AEDs have an established therapeutic drug concentration to monitor, and the researchers in the above study provided education only to patients who received the AED Valproic acid which makes their results only applicable to this specific type of patients (24). Chen *et al*(2013) evaluated the effect of education by pharmacist on caregiver's knowledge about epilepsy, and it was found to increase the caregivers' knowledge significantly, but it did not correlate the effect of this increase in knowledge with the efficacy of treatment as this study did, and it had a sample size of 27 caregivers only (8). A significant direct correlation was found in our study between the number of seizures and the number of AEDs prescribed to the patient and this is expected as when the patient is experiencing more seizures, he will be prescribed more AEDs to control them.

4.2 Safety

The education was not presumed to decrease the severity of side effects directly, especially those related to cognition, coordination and academic performance, but with gaining more knowledge about the side effects of AEDs, the patients and their caregivers will report them more considerably and will not overestimate the non-specific side effects like headache and tiredness. As a result of better understanding of the medications' side effects, caregivers in this study also reported new side effects experienced by their children to the neurologist and clinical pharmacist after receiving the education, which is probably attributed to more motivation to report any experienced side effect during the educational session. Side effects score was found to be significantly and inversely correlated with QoL, which expected since as side effects increases, the quality of life of the patient will be diminished. It was also directly correlated with number of medications (i.e. AEDs) at both baseline and follow-up, as when the patient is prescribed more medications, he/she will experience more side effects.

Our results are similar to those observed by May *et al.* (2002) which was, as mentioned above, a study that evaluated the effect of MOSES educational program on PWE with regard to different aspects including knowledge about medications and reporting of their ADR. Better knowledge about therapy resulted in better tolerability of AEDs and ability to differentiate between a non-specific complaints that is not related to AED therapy and an actual ADR from AEDs. Patients were also more encouraged to ask about their medications and to get more information about side effects (23). Results of our study were also consistent with those

reported by Moura *et al* . (2016) who evaluated the effect of education about AEDs side effects on adherence and concluded that, despite knowledge about the possible side effects of AEDs, it did not affect their reported adherence to medications (25).

4.3 Adherence

Several previous studies were done to evaluate the effect of education on adherence. Unlike ours, Ibinda *et al.* (2014) found no significant difference between the control and intervention group with regard to adherence, either by monitoring AEDs' blood levels or self-reported adherence. Adherence increased significantly in both groups and this may be due to sharing knowledge between participants as reported by the authors (22).

On the other hand, the results of our study are consistent with the results of previous ones that emphasized the positive effect of education on adherence to AEDs in intervention group. Ma *et al* . (2019) found that adherence increased from 56% to 73.9% after education (24), and Tang *et al* (2014) also found an increase in patients with high level of adherence after education from 7.5% to 60.4%, and the overall percentage of patients that their adherence increased were 62.3% (P-value <0.0001) (9). Fogg *et al* . (2012) also reported a significant increase in patients reporting adherence and never deviating from administering medication after education provided by a pharmacist (P -value <0.03) (26). These results indicate that patient's or caregiver's level of adherence to medications for his/her family member can be increased significantly by providing information through an appropriate method of education, and the clinical pharmacist can be the provider of this education material. The clinical pharmacist has the ability to establish an administration schedule and record of medication administration, and follow up with patients regarding their medications and treatment plan. Interestingly, adherence at follow-up was significantly correlated with QoL which indicates that a better adherence is associated with a better QoL.

4.4 Satisfaction with information about AEDs

With regard to satisfaction with information about AEDs, the results of this study were consistent with those of Fogg *et al.* (2012) study that evaluated the effect of pharmacist-led epilepsy consultation on patients' satisfaction with information received about epilepsy medications, that increased the overall satisfaction from 11 to 13 (P- value= 0.009) (26).

The increase in satisfaction in this study was also associated with a significant increase in the level of adherence. Not only adherence, but also safety and QoL was associated with satisfaction. At follow-up, an inverse relationship was found between satisfaction and safety, this means that when satisfaction with information about AEDs increased, it led to a lower side effects score indicating better understanding of drugs side effects. On the other hand, a direct relationship between satisfaction and QoL indicates that better understanding about the medication effects, either the wanted or unwanted (side effects), led to a higher QoL score.

In this study, the control group also experienced a statistically significant increase in the level of satisfaction at follow up, although no new information was provided to patients or caregivers during the study period, this may be due to social desirability bias as the clinical pharmacist frequently contacted the caregiver to receive relevant study information.

4.5 Quality of life

The change which was observed in both groups during a relatively short period of follow up may be due to actual deterioration or improvement of certain QoL subscales like executive function or mood, as these effects relatively can change in this short period of time. Education on its own is not expected to significantly change the patients QoL, especially that the education in our study was only done once and for 30 minutes, multiple educational sessions over several time intervals may have a more pronounced effect on QoL.

QoL was correlated with several study outcomes, this implies that the utmost results of patient treatment are seen in his/her Qol. Nevertheless, QoL also significantly correlated with different demographic and clinical characteristics of patients, an inverse relationship with age, siblings with epilepsy, and number of AEDs at

both baseline and follow-up, this means that when the child is olderm when he/she has siblings with epilepsy, and when he/she is taking more AEDs, the effect on his/her QoL is more prominent,

The results of our study are similar to those described by Fogg *et al* . (2012) who found an improvement in patients' QoL after providing a pharmacist consultation session (26), while May *et al.* (2002) found significant effect only on the mental component of QoL but no significant difference on the physical component of QoL (23). This further adds to the evidence of improving QoL in pediatric patients with epilepsy after performing an educational session.

5 CONCLUSION

Pharmacist-led education about epilepsy and AEDs can potentially increase the efficacy and safety of AEDs but this increase was not significant from the control after an eight-week follow-up. Although the baseline level of adherence in pediatric patients with epilepsy was moderate and level of satisfaction in caregivers about AEDs was low but they both significantly increased in intervention group after education provided by the clinical pharmacist, and was significantly higher than that of the control. Quality of life in pediatric patients with epilepsy was compromised according to their caregivers' opinion, but has been shown to increase when pharmacist-led education is provided about their disease and medications, so the clinical pharmacist plays a pivotal role in the care of pediatric patients with epilepsy and thus should be included in the healthcare team for these patients.

Tables:

Table 1. Baseline demographic and clinical characteristics of study participants

Variable	Variable	Variable	All participants (n=81)	Intervention group (n= 41)	Control group (n=40)	*P*- value
Gender; n (%)	Gender; n (%)	Male	47 (58.0%)	21 (51.2%)	26 (65.0%)	0.21
		Female	34 (42.0%)	20 (48.8%)	14 (35.0%)	
Residence; n (%)	Residence; n (%)	Amman	29 (35.8%)	17 (41.4%)	12 (30%)	0.45
		Irbid	13 (16.1%)	5 (12.25%)	8 (20%)	
		Balqa	10 (12.4%)	5 (12.25%)	5 (12.5%)	
		Others	29 (35.8%)	14 (34.1%)	15 (37.5%)	
Education (Caregiver); n (%)	Education (Caregiver); n (%)	University	14 (17.3%)	9 (22%)	5 (12.5%)	0.02
		College	14 (17.3%)	10 (24.4%)	4 (10%)	
		Tawjihi	37 (45.6%)	15 (36.6%)	22 (55%)	
		Less than Tawjihi	16 (19.8%)	7 (17%)	9 (22.5%)	
Monthly income; n (%)	Monthly income; n (%)	(0-500)	12 (14.8%)	5 (12.2%)	7 (17.5%)	0.5
		(500-1000)	69 (85.2%)	36 (87.8%)	33 (82.5%)	
Presence of medical insurance; n (%)	Presence of medical insurance; n (%)	Yes	79 (97.5%)	41 (100%)	38 (95.0%)	0.15
		No	2 (2.5%)	0 (0%)	2 (5.0%)	
Family history of epilepsy; n (%)	Family history of epilepsy; n (%)	Yes	17 (21.0%)	7 (17.1%)	10 (25.0%)	0.38

Variable	Variable	Variable	All participants (n=81)	Intervention group (n= 41)	Control group (n=40)	*P*- value
		No	64 (79.0%)	34 (82.9%)	30 (75.0%)	
Presence of sibling with epilepsy; n (%)	Presence of sibling with epilepsy; n (%)	Yes	6 (7.4%)	4 (9.8%)	2 (5.0%)	0.25
		No	75 (92.6%)	37 (90.2%)	38 (95.0%)	
Number of chronic diseases; n (%)	Number of chronic diseases; n (%)	One (only epilepsy)	76 (93.8%)	37 (90.2%)	39 (97.5%)	0.04
		Two	5 (6.2%)	4 (9.8%)	1 (2.5%)	
Presence of drug allergy; n (%)	Presence of drug allergy; n (%)	Yes	6 (7.4%)	4 (9.8%)	2 (5.0%)	0.41
		No	75 (92.6%)	37 (90.2%)	38 (95.0%)	
Number of medications; n (%)	Number of medications; n (%)	One	43 (53.1%)	19 (46.3%)	24 (60.0%)	0.51
		Two	21 (25.9%)	11 (26.8%)	10 (25.0%)	
		Three	15 (18.5%)	10 (24.4%)	5 (12.5%)	
		Four	2 (2.5%)	1 (2.4%)	1 (2.5%)	
AED; n (%)	AED; n (%)	VPA	47 (58%)	27 (65.8%)	20 (50%)	-
		LEV	38 (46.9%)	16 (39%)	22(55%)	
		CBZ	15 (18.5%)	7 (17%)	8 (20%)	
		TPM	10 (12.3%)	8 (19.5%)	2 (5%)	
Age (Years); n (%)	0-6	0-6	27 (33.3%)	16 (39%)	11 (27.5%)	0.54
	7-12	7-12	37 (45.7%)	17 (41.5%)	20 (50%)	
	13-18	13-18	17 (21%)	8 (19.5%)	9 (22.5%)	
Weight; Mean(SD)	Weight; Mean(SD)	Weight; Mean(SD)	30.3 (14.5)	29.35 (13.7)	31.3 (15.5)	0.65
Height; Mean(SD)	Height; Mean(SD)	Height; Mean(SD)	118.4 (26.4)	119.7 (25.5)	117 (27.5)	0.55

AED: antiepileptic drug, VPA: Valproate, LEV: Levetiracetam, CBZ: Carbamazepine, TPM: Topiramate

Table 2. Main Outcomes results

Difference between baseline and follow-up

Outcome	**Control group Baseline (n=40)**	**Control group Follow-up (n=35)**	**Control group** *P*-**value**	**Intervention group Baseline (n=41)**	**Intervention group Follow-up (n=36)**	**Intervention group** *P*-**value**
Efficacy^{+} n (%)	11 (27.5%)	17 (48.6%)	<0.05*	13 (31.7%)	23 (63.9%)	<0.001**
Safety^{++} Mean (SD)	21.42 (12.16)	23.73 (13.24)	<0.001**	21.08 (10.59)	18.91 (9.44)	<0.001**

Adherence§ Mean (SD)	6.05 (1.26)	5.85 (1.43)	>0.05	6.04 (1.09)	7.61 (0.9)	<0.001**
Satisfaction¶ Mean (SD)	2.2 (2.76)	2.66 (2.68)	<0.05*	0.76 (1.4)	12.58 (1.4)	<0.0001**
QoL Mean (SD)	70.88 (20.7)	64.63 (21.58)	<0.05*	70.75 (14.5)	75.09 (14.87)	<0.001**
Difference between groups at follow-up	Difference between groups at follow-up	Difference between groups at follow-up	Difference between groups at follow-up	Difference between groups at follow-up	Difference between groups at follow-up	Difference between groups at follow-up
Outcome	**Control group**	**Control group**	**Control group**	**Intervention group**	**Intervention group**	***P*-value**
Efficacy+	17 (48.6%)	17 (48.6%)	17 (48.6%)	23 (63.9%)	23 (63.9%)	>0.05
Safety++	23.73 (13.24)	23.73 (13.24)	23.73 (13.24)	18.91 (9.44)	18.91 (9.44)	>0.05
Adherence§	5.85 (1.43)	5.85 (1.43)	5.85 (1.43)	7.61 (0.9)	7.61 (0.9)	<0.0001**
satisfaction¶	2.66 (2.68)	2.66 (2.68)	2.66 (2.68)	12.58 (1.4)	12.58 (1.4)	<0.0001**
QoL	64.63 (21.58)	64.63 (21.58)	64.63 (21.58)	75.09 (14.87)	75.09 (14.87)	<0.05*

+ Number of seizure free patients ++ Pediatric epilepsy side effects questionnaire score § Morisky medication adherence score ¶ Satisfaction with information about medicines score * statistically significant at the level of P -value <0.05 ** statistically significant at the level of P -value <0.01

Table 3. Correlation between study outcomes

	Baseline	Baseline	Follow-up	Follow-up
Study outcomes	**r**	***P*-value**	**r**	***P*-value**
Efficacy+ and safety++	0.013	0.914	0.018	0.885
Efficacy+ and adherence§	0.194	0.106	-0.043	0.721
Efficacy+ and satisfaction¶	0.164	0.171	0.021	0.865
Efficacy+ and QoL	-.055	0.646	-0.178	0.137
Safety++ and adherence§	-0.06	0.62	-0.214	0.074
Safety++ and satisfaction¶	-0.112	0.354	-0.263	<0.05*
Safety++ and QoL	-0.723	<0.0001**	-0.782	<0.0001**
Adherence§ and satisfaction¶	0.173	0.15	0.682	<0.0001**
Adherence§ and QoL	-.063	0.6	0.323	<0.01**
Satisfaction¶ and QoL	-.053	0.66	0.298	<0.05*

+ Number of seizures ++ Pediatric epilepsy side effects questionnaire score § Morisky medication adherence score ¶ Satisfaction with information about medicines score * statistically significant (Pearson correlation test) at the level of P -value <0.05 ** statistically significant (Pearson correlation test) at the level of$P$ -value <0.01

Table 4 Significant correlation between the study outcomes and patients' demographic and clinical characteristics

Study Outcome	Baseline QoL	Follow-up QoL	Baseline safety	Follow-up safety	Follow-up efficacy
Variable					
Age	r=-0.413	-	-	-	-

Study Outcome	Baseline QoL	Follow-up QoL	Baseline safety	Follow-up safety	Follow-up efficacy
Siblings with epilepsy	*P*-value <0.0001** r=-0.276	-	-	-	-
Number of medications	*P*-value < 0.05* r=-0.421	r=-0.409	r=0.318	r=0.259	r=0.240
	P-value <0.0001**	*P*-value <0.0001**	*P*-value <0.01**	*P*-value <0.05**	*P*-value <0.05**

* Statistically significant (Pearson correlation test) at the level of$P$ -value <0.05 ** statistically significant (Pearson correlation test) at the level of P -value <0.01

Figure legends

Figure 1. Study design: controlled, randomised study

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Figure 3. Seizure status in study participants at baseline and follow up

Figure 4. Mean outcome measures for safety, adherence, satisfaction with information about AEDs and QoL in study participants; AED: Antiepileptic drug, QoL: Quality of life

Figure 5. Level of adherence in study participants

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Data availability statement

The data that support the findings of this study are available upon request from the corresponding author. The data are not publicly available due to privacy or ethical considerations.

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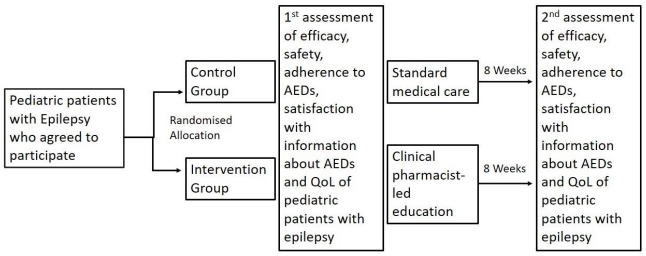

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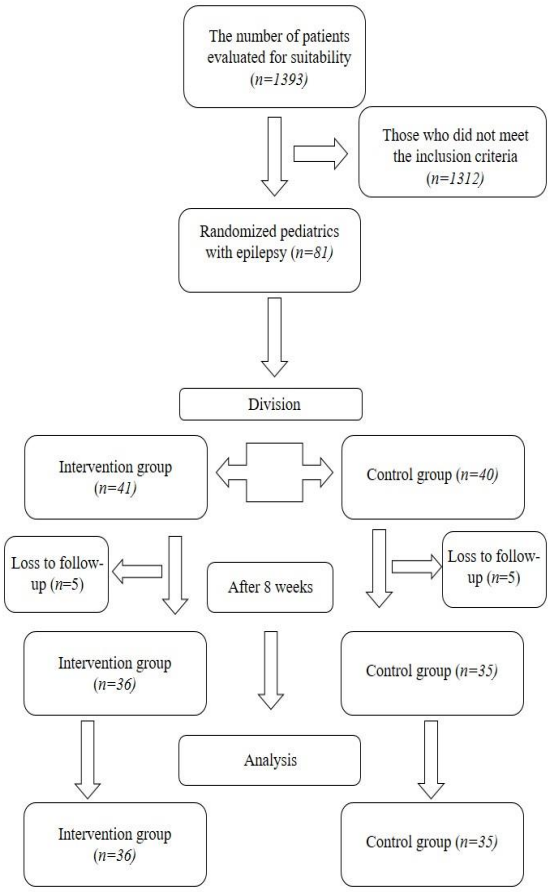

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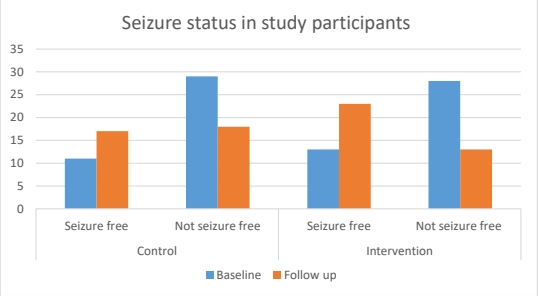

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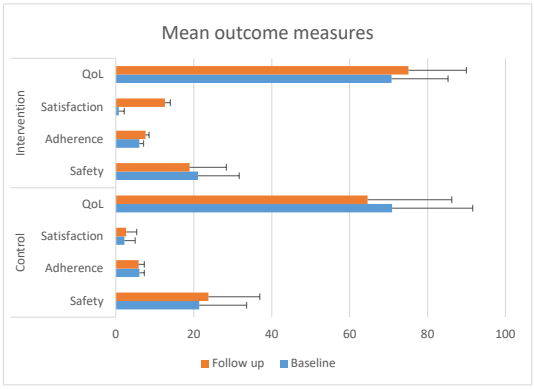

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