

Adherence to Antiepileptic Drugs and the Health Literacy of Caregivers in Childhood Epilepsy

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Objective: To investigate the relationship between caregivers' health literacy and adherence to treatment in children with epilepsy.

Methods: The participants included 226 children and adolescents with epilepsy and their primary caregivers. The demographic and clinical characteristics were abstracted. An antiepileptic drug adherence assessment was done with the validated Morisky Medication Adherence Scale-8 (MMAS-8). According to the scale's scoring system, 0 points indicates high adherence, 1 to 2 points, moderate adherence, and 3 to 8 points, low adherence. A 17-item public health literacy knowledge scale (PHLKS) was used to measure the caregivers' levels of health knowledge. For this scale, higher scores indicate higher levels of health knowledge. A logistic regression model was used to evaluate the effects of demographic characteristics and clinical findings on full drug adherence.

Results: The overall prevalence of complete drug adherence among patients was 47.3%. The median value of the MMAS-8 score was 1 point (0–8 points). The main reasons for high scores were forgetting to take medication (33.6%) and the difficulties in adhering to treatment (24.3%). The median of the PHLKS score was 13 points (4–17 points). According to the logistic regression results, patients in the 0 to 5 years age group were more likely to have full drug adherence than were those in the 12 to 18 years age group (OR [95% CI]: 2.9 [1.4–6.5]; $p = 0.007$). As the PHLKS score increased, drug adherence also significantly increased (OR [95% CI]: 0.8 [0.7–0.9]; $p = 0.008$).

Conclusion: Age and caregivers' health literacy knowledge were found to be significantly associated with adherence. To better define the factors associated with drug adherence in children with epilepsy, additional research (using objective, validated tools) aimed at determining caregivers' health literacy is needed. [*P R Health Sci J* 2020;39:45-50]

Key words: Adherence, Epilepsy, Health literacy, Children

Epilepsy is a serious but treatable neurological disorder characterized by recurrent spontaneous seizures. It affects approximately 1% of children (1,2). Antiepileptic drugs (AEDs) are the primary treatment for most epilepsy patients. The main goal of treatment is to increase quality of life by reducing the frequency of seizures while keeping the side effects of these AEDs at a minimum (3). Almost 70% of newly diagnosed epileptic patients live seizure free with appropriate and effective AEDs (4).

The underlying mechanism of persistent seizures in epileptic patients has not been fully elucidated, yet. However, non-adherence to AEDs has been shown to contribute to the persistence of seizures and yet is an entirely modifiable factor (1). Previous studies have reported that 58% of epileptic children do not fully adhere to therapy in the first 6 months of treatment. Moreover, at 4-year follow-up after diagnosis, the frequency of repeated seizures has been shown to be 3.2

times higher in AED–non-adherent patients than in those who are AED adherent (5,6). AED non-adherence leads to increases in admissions to emergency rooms in the frequency of accidents, injuries, and hospitalization; and in health-care costs and morbidity and mortality rates, any of which (singly or in combination) can cause a decrease in a given patient's quality

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The author/s has/have no conflict/s of interest to disclose.

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of life and negatively affect that patient's caregiver(s), socially, economically, and/or psychologically (7).

Clinicians should work cautiously to reduce the side effects that can, potentially, provoke decreased drug adherence and, thus, lessen the efficacy of a given AED (8). Defining factors that contribute to AED non-adherence may lead to the development of interventions that increase adherence and improve clinical outcomes (9). Many researchers have studied—using a variety of scales—drug adherence in epileptic patients. The most valid method for doing so is a self-report scale such as the Morisky Medication Adherence Scale (MMAS-4 and MMAS-8) (8).

UNESCO defines literacy as “the ability to identify, understand, interpret, create, communicate and compute, using printed and written (and visual) materials associated with varying contexts” (10). In chronic disorders such as epilepsy, parental literacy is important for compliance with medical treatment (11). According to UNESCO data from 2012, 781 million adults, worldwide, lack basic literacy skills. Adult literacy rates have increased over the last decade but still have not reached the targeted level, especially in women (89% for men and 80% for women). Sixty-four percent of illiterate adults are women (12). Considering the fact that the caregivers of children with any kind of chronic disorder are usually women, this situation should be regarded as an essential impediment to the success of any treatment.

Public health literacy is a complement to individual health literacy (13). The health literacy levels of individuals can be assessed with various scales. (14–16). As the level of health literacy increases, the levels of knowledge, motivation, and proficiency that enable people to access, understand, evaluate, and use health information also increase. As a consequence, individuals make decisions about and work on their health in their daily lives and increase the quality of those lives by improving their general health status and preventing diseases. (15). The aim of our study was to investigate the relationship between drug adherence and caregiver health literacy in pediatric patients with epilepsy.

Materials and Methods

This study was carried out with 226 epileptic patients from 3 months to 18 years of age who were admitted to the Bursa Yuksek Ihtisas Training and Research Hospital, Department of Pediatric Neurology, from January 2018 through September 2018.

Inclusion criteria: 1) being from 3 months to 18 years old, 2) having been diagnosed with epilepsy and using at least 1 AED, 3) being willing to comply with the study procedures, and 4) giving written informed consent. Those who had any type of comorbid disease and/or developmental disorder and those who did not agree to participate in the study were excluded.

After the approval of the study by the Clinical Trials Ethics Committee (2011-KAEK-25 2018/08-13), the participating caregivers were asked to complete the informed consent and demographic forms during the enrollment of the patient. Epilepsy is defined as having 2 or more episodes of unprovoked seizures

occurring at least 24 h apart. For each of the study's participants, a qualified pediatric neurologist established the diagnosis of epilepsy with a detailed anamnesis, a neurological examination, electroencephalography (EEG), and neuroimaging (i.e., computed tomography, magnetic resonance imaging). Patients who had had no seizures for at least 1 year without any changes in their treatment were considered to be “seizure free.” Drug-resistant epilepsy was defined as having an inadequate response to 2 different AEDs which were appropriately selected and used.

The gender, age, caregiver status (age, educational attainment, etc.), duration of epilepsy, AEDs used, treatment changes, and the type and frequency of seizures of and for all the participants were noted.

To assess drug adherence in the participants, the Turkish version of the MMAS-8 questionnaire (17) was used. It consists of 8 items and uses the following scoring scheme: for the first 6 items, “Yes” = 0 and “No” = 1; for the seventh item, “Yes” = 1 and “No” = 0; for the eighth item, “No/never” = 0 and other answers = 1. The scores for all the items are summed to give a range of scores, from 0 to 8 points. In terms of the total score, a score of 0 indicates high adherence, a score of 1 to 2, moderate adherence, and a score of 3 to 8, low adherence. A patient with an MMAS-8 score of 0 points was defined as being “completely drug adherent.”

The Turkish version of the 17-item public health literacy knowledge scale (PHLKS) developed by Pleasant and Kuruvilla (16) was used to measure each caregiver's level of health knowledge. Each item was answered with “right” or “wrong.” The evaluation was made according to the total score. A higher score indicates a higher level of knowledge on health. The MMAS-8 and PHLKS are administered in written forms but can be administered orally if the participant is illiterate.

Statistical analysis

IBM SPSS (Statistical Package for the Social Sciences) Statistics for Windows, version 21.0, was used for the data analysis. Categorical variables were expressed as n (%); normally distributed continuous variables, as mean \pm SD; and non-normally distributed continuous variables, as median (minimum–maximum). A univariate analysis with the chi-square or Fisher's exact test was used to observe associations between the demographic data, the clinical findings, and adherence.

Multivariate analysis was conducted using logistic regression to evaluate the effects of associated factors on full drug adherence. Ninety-five percent confidence intervals were calculated for each variable. A p value of less than 0.05 was considered statistically significant.

Results

Patient characteristics

Four hundred fifty-five patients with epilepsy admitted to our pediatric neurology department were evaluated during the study period. As we excluded patients with a comorbid disease or who did not agree to participate in the study, a total of 226

children formed the study population. The median age was 103 months (min–max = 10–216 months) in the study group. The male/female ratio was 1.05 (116/110). Primary caregivers were, mostly, mothers (90.7%). The majority (69%) of the initial AED prescriptions were for valproate. Forty-four (19.5%) of the patients had been prescribed one of the new generation drugs, and 31 (13.7%) were being treated with combination therapy. The detailed demographic and clinical characteristics of the patients are summarized in Table 1.

Treatment resistance

The interview data revealed that the median self-reported seizure frequency was 0.14 times/month (min–max = 0–2.7 times/month) over the course of the disorder to present day. There

Table 1. Demographic and clinical characteristics of the patients with epilepsy.

Variable	n (%)
<i>Age (years)</i>	
0–5 (toddler–early childhood)	59 (26.2)
6–11 (middle childhood)	95 (42)
12–18 (adolescent)	72 (31.8)
<i>Sex</i>	
Male	116 (51.3)
Female	110 (48.7)
<i>Participating caregiver</i>	
Mother	205 (90.7)
Father	19 (8.4)
Other	2 (0.9)
<i>Caregiver's educational status</i>	
Unable to read and write	19 (8.4)
Primary school	117 (51.8)
Secondary school	77 (34)
Diploma and above	13 (5.8)
<i>Duration of epilepsy (years)</i>	
<1	35 (15.4)
≥1	191 (84.6)
<i>Type of epilepsy</i>	
Focal	11 (4.8)
Generalized	215 (95.2)
<i>Type of AED therapy</i>	
Monotherapy	182 (80.5)
Polytherapy	44 (19.5)
<i>Type of AED used</i>	
Old	151 (66.8)
New	44 (19.5)
Combination	31 (13.7)
<i>Initial AED</i>	
Valproate	156 (69)
Levetiracetam	38 (16.8)
Phenobarbital	11 (4.9)
Carbamazepine	9 (4)
Oxcarbazepine	5 (2.2)
Lamotrigine	2 (0.9)
Topiramate	2 (0.9)
Clonazepam	1 (0.4)
Phenytoin	1 (0.4)
Vigabatrin	1 (0.4)
<i>Treatment resistance</i>	
Yes	21 (9.2)
No	205 (90.8)

were 21 patients (9%) with treatment-resistant epilepsy. When the treatment-resistant patients were compared with the other patients in terms of age ($p = 0.8$), gender ($p = 0.1$), caregiver education status ($p = 0.5$), duration of epilepsy ($p = 0.4$), type of epilepsy ($p = 0.3$), type of AED therapy ($p = 0.7$), type of AED used ($p = 0.6$), PHLKS score ($p = 0.2$), and MMAS-8 score ($p = 0.4$), there was no statistically significant difference between the groups.

Treatment adherence and Public health literacy levels

The median value of the MMAS-8 score of the patients was 1 point (min–max = 0–8 points). The main reasons for high scores were forgetting to take medication (33.6%) and the difficulties in adhering to treatment (24.3%). The median of the PHLKS score was 13 points (min–max = 4–17 points). The most common incorrect answers to the respective questions were: *The use of mosquito nets can prevent malaria* (40.4%), and *All bacteria are harmful to humans* (45.6%). The overall prevalence of complete drug adherence among the patients was 47.3%. Age and PHLKS score were found to be associated with full adherence ($p = 0.03$ and $p = 0.005$, respectively). Gender, caregiver educational status, duration of epilepsy, type of epilepsy, type of AED therapy, and type of AED used were not significantly associated with AED adherence (Table 2).

Table 2. Results of univariate analysis comparing adherent and non-adherent patients

Characteristic	Complete medication adherence		P-value
	Yes	No	
<i>Total unique patients, n (%)</i>	107 (47.3)	119 (52.7)	
<i>Age in months, median (min–max)</i>	96 (12–204)	112 (10–216)	0.03
<i>Sex, n (%)</i>			0.5
Male	57 (25.2)	59 (26.1)	
Female	50 (22.2)	60 (26.5)	
<i>Caregiver's educational status, n (%)</i>			0.6
≤ Middle school	61 (26.9)	75 (33.2)	
≥ High school	46 (20.4)	44 (19.5)	
<i>Duration of epilepsy in years, n (%)</i>			0.2
<1	29 (12.8)	24 (10.6)	
≥1	78 (34.6)	95 (42)	
<i>Type of epilepsy n (%)</i>			0.8
Focal	8 (0.4)	3 (0.18)	
Generalized	99 (43.8)	116 (51.3)	
<i>Number of AEDs, median (min–max)</i>	1 (1–3)	1 (1–4)	0.4
<i>Type of AED therapy, n (%)</i>			0.3
Monotherapy	89 (39.3)	93 (41.1)	
Polytherapy	18 (8.1)	26 (11.5)	
<i>Type of AED used, n (%)</i>			0.1
Old	79 (34.9)	72 (31.8)	
New	16 (7.2)	28 (12.4)	
Combination	12 (5.3)	19 (8.4)	
<i>Drug resistant epilepsy, n (%)</i>			0.3
Yes	8 (3.5)	13 (5.8)	
No	99 (43.8)	106 (46.9)	
<i>PHLKS, median (min–max)</i>	14 (6–17)	13 (4–17)	0.005

Univariate analysis showed that age and PHLKS score were related to drug adherence. Therefore, these 2 factors were included in the multiple logistic regression analysis, along with other factors considered to affect drug adherence (caregiver's educational status, duration of epilepsy [years], type of AED therapy, type of AED used, and type of epilepsy). According to the logistic regression results, patients in the 0 to 5 years age group were more likely to have full drug adherence than were those in the 12 to 18 years age group (OR [95% CI]: 2.9 [1.4–6.5]; $p = 0.007$). As the PHLKS score increased, drug adherence also significantly increased (OR [95% CI]: 0.8 [0.7–0.9]; $p = 0.008$). The results of the multiple logistic regression analysis are summarized in Table 3.

Table 3. Results of the logistic regression analysis evaluating the factors associated with non-adherence

Variable	B	p-value	OR (95% CI)
Age (years)		0.025	
0–5 (toddler–early childhood)		Reference	
6–11 (middle childhood)	0.56	0.1	1.7 (0.9–3.5)
12–18 (adolescent)	1.08	0.007	2.9 (1.4–6.5)
Caregiver's educational status	0.25	0.5	1.3 (0.7–2.5)
Duration of epilepsy (years)	0.23	0.5	1.3 (0.7–2.4)
Type of AED therapy	0.85	0.8	1 (0.5–2.3)
Drug resistant epilepsy	-0.29	0.6	0.8 (0.3–2)
Public health literacy knowledge scale	-0.2	0.008	0.8 (0.7–0.9)

B: regression coefficient; OR: odds ratio; CI: confidence interval. Adherence coded as 0; non-adherence coded as 1

Discussion

Epilepsy is one of the most important disabling neurological conditions of childhood, but it is still not considered a serious public health problem. Regular usage of AEDs is an important part of the treatment for epilepsy. This study aimed to investigate parental health literacy levels and other factors that may be associated with drug adherence in pediatric patients with epilepsy.

The AED adherence rates in children with epilepsy vary from 22.1% to 96.5% because of the different methods used in different studies (18). In our study, the rate of full drug adherence in our epileptic patients was 47.3%.

In some of the previous studies evaluating drug adherence in pediatric epileptic patients (19–21), age was reported to be associated with drug adherence. Shah et al. (19) and Shetty et al. (20) reported that drug adherence decreased as the patient's age increased; on the other hand, Lee et al. (2) stated that drug adherence was significantly lower in toddlers compared to adolescents. Jacob et al. (21) studied 5214 children with epilepsy, and they found that in children under 5 years of age, drug adherence was better than it was in patients in the age group of 14 to 17 years. Differences in the population, including age, may partially explain this seeming discrepancy. Some studies have included prevalent AED users (with a median duration of

epilepsy of 4 years); some have included incident AED users. In addition, some studies have included age at first AED treatment as a variable. There may also be a difference in patients' concerns about seizure recurrence between patients who experienced epilepsy onset in adolescence and those whose onset occurred during their first years of life. In our study, we observed that drug adherence was better in toddlers than adolescents. These results suggest that drug adherence is better in the 5-year-old age group because drugs are given by the patients' caregivers, while adolescents usually manage their own treatment.

In our study, a large percentage of patients suffered from generalized epilepsy. Shah et al. (19) reported that drug adherence was lower in patients with generalized epilepsy than it was in other patients with epilepsy. Al-Faris et al. (22) concluded that drug adherence in generalized epilepsy patients with absence seizures was better than it was in patients with febrile, Rolandic or myoclonic seizures. In our study, we did not find any relationship between drug adherence and the type of seizure.

For the patients in our study, the majority of the initial AED prescriptions were for valproate. Lee et al. (2) reported that drug adherence was higher with the new generation of drugs than it was with the older generations. In our study, there was no relationship between drug adherence and the generation to which a specific drug belonged.

In the previous studies, there has been an inconsistent relationship reported between the number of drugs used and treatment adherence. Carbone et al. (23) found that drug adherence increased as the number of drugs increased; whereas Gabr and Shams et al. (24) reported the opposite. In our study, there was no relationship between single or multiple drug intake and drug compliance.

In their study on 63 children with epilepsy, Alsous et al. (25) found that drug adherence decreased as the duration of the disorder increased. In our study, there was no relationship between drug adherence and said duration.

Although epilepsy is a common disorder and there are many studies on drug adaptation, there are limited data on the relationship between the health literacy of caregivers and drug compliance in patients with epilepsy. For some of the chronic diseases, disorders, and conditions that occur in childhood, there are studies showing a relationship between drug adherence and the health literacy of caregivers. For instance, the low health literacy of caregivers caring for children with asthma and insulin-dependent diabetes mellitus was found to be associated with lower drug adherence (26,27). In previous studies on epilepsy, the levels of caregiver knowledge about the disorder and compliance with treatment have been investigated; however, there is a gap in the literature about the relationship between general health literacy levels and drug compliance (23,24). Addressing this issue, the study by Paschal et al., conducted with a total of 146 pediatric patients with epilepsy and their families and caregivers, is noteworthy, in that Paschal and her team examined the relationship between general health literacy levels and drug compliance. Paschal et

al. (11) reported that inadequate health literacy in caregivers/families is an independent risk factor for unfavorable outcomes associated with drug non-adherence in pediatric patients with epilepsy. In our study, we found that as the levels of caregiver health literacy increased, drug adherence also significantly increased.

There are some limitations to our study. Even though MMAS-8 is a validated and widely accepted scale for the assessment of drug adherence, it is a subjective method and tends to show higher adherence because it is filled out by caregivers.

One of the limitations pertains to the sample size; additionally the study was not designed with a specific power, which limits the generalizability of the study findings. Nonetheless, further research, using comparative groups and larger representative sample sizes, is recommended. Another limitation of this study relates to the number of factors or predictors which were investigated, some of which either already have been or might be associated with the issue of adherence but that we did not assess in our study; included among them are family socioeconomic status, comorbid and developmental disorders, medication side effects, and cultural factors. In addition the study did not include the number of dosing times per day as a study variable. This factor may have had an impact on adherence that has yet to be measured. Further, the majority of patients suffered from generalized epilepsy. Adherence rates may be different for other pediatric epilepsy syndromes.

The relationship between caregiver health literacy and drug adherence in pediatric patients with epilepsy has not been studied extensively. The most powerful aspect of our study is the revealing of this relationship. Despite the study's limitations, we believe that our study findings make a significant contribution to the current literature on this topic.

Conclusion

For children with epilepsy, AED compliance is critical. There is a need for further studies exploring those factors that are independently associated with drug compliance. In our study, the logistic regression analysis showed that patients in the 0 to 5 years age group were more likely to have full drug adherence than were those in the 12 to 18 years age group; and as the PHLKS score increased, drug compliance also significantly increased.

It is known that long-term drug adherence is more difficult in chronic disorders, especially for adolescents. The importance of drug adherence can be underestimated by parents with low education levels. Clinicians should emphasize the importance of drug adherence at every visit because such emphasis can increase adherence and, thus, treatment success.

A better understanding of the relationship between caregiver health literacy and drug adherence may lead to the provision of better care and treatment for children with epilepsy. Large-scale, multicenter studies using objective, validated tools are needed to define the factors associated with drug adherence in children with epilepsy.

Resumen

Objetivo: Falta información sobre la relación entre el conocimiento sobre la salud de los cuidadores y la adherencia al tratamiento en niños con epilepsia. El objetivo de este estudio fue investigar la relación entre el nivel de conocimiento en salud de los cuidadores y la adherencia al fármaco en pacientes pediátricos con epilepsia. **Métodos:** Los participantes incluyeron 226 niños y adolescentes con epilepsia y sus cuidadores principales. Se resumieron las características demográficas y clínicas. La evaluación de la adherencia al fármaco antiepiléptico se realizó mediante la Escala de Adherencia a la Medicación de Morisky-8 ítems validada (MMAS-8, por sus siglas en inglés). De acuerdo al sistema de puntuación de dicha escala, 0 puntos indica adherencia alta, 1-2 puntos indica adherencia moderada y 3-8 puntos indica adherencia baja. Se utilizó una escala de conocimiento de alfabetización de salud pública de 17 ítems (PHLKS, por sus siglas en inglés) para medir el nivel de conocimiento de salud de los cuidadores. Se utilizó un modelo de regresión logística para evaluar los efectos de los datos demográficos y los hallazgos clínicos en la adherencia total al fármaco. **Resultados:** La prevalencia general de adherencia completa al fármaco entre los pacientes fue del 47.3%. El valor medio de la puntuación MMAS-8 fue de 1 punto (0-8 puntos). Las razones de las puntuaciones altas fueron en su mayoría olvidar tomar la medicación (33.6%) y las dificultades en la adherencia al tratamiento (24.3%). La mediana de la puntuación de PHLKS fue de 13 puntos (4-17 puntos). De acuerdo con los resultados de la regresión logística, los pacientes en el grupo de 0 a 5 años de edad tenían más probabilidades de tener una adherencia total al fármaco que el grupo de 12 a 18 años de edad [OR (95% IC): 2.9 (1.4-6.5), $p = 0.007$]. A medida que aumentó la puntuación de PHLKS, la adherencia al fármaco también aumentó significativamente [OR (IC del 95%): 0.8 (0.7-0.9), $p = 0.008$]. **Conclusión:** Se encontró que la edad y los conocimientos en salud de los cuidadores estaban significativamente asociados con la adherencia. Para definir mejor los factores asociados con la adherencia a los medicamentos en niños con epilepsia, se necesita investigación adicional (utilizando herramientas objetivas y validadas) para determinar el conocimiento en salud de los cuidadores.

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