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ORIGINAL ARTICLE

Pharmacist's Impact on Medication Adherence and Drug-Related Problems in Patients with Epilepsy

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ABSTRACT

Objectives: Drug-related problems (DRPs) and non-adherence are important barriers to ensuring optimal antiseizure drug treatment. The aim of this study was to improve medication adherence, detect and manage DRPs, and decrease the number of seizures with pharmacist-led education in patients with epilepsy.

Materials and Methods: A prospective and interventional study was conducted in collaboration with the Department of Neurology, the rational drug usage unit of a hospital pharmacy in a university hospital. The impact of pharmacist-led education on medication adherence and interventions in the management of DRPs was assessed in patients with epilepsy who were admitted to the outpatient clinic. A total of 39 patients with epilepsy were evaluated in terms of medication adherence, DRPs, and seizure control over a 2-month follow-up period and patient satisfaction with pharmacy services at the end of the study.

Results: A total of 59 DRPs were detected, and 71.2% of them were accepted and implemented both by physicians and/or patients. Pharmacist interventions solved 62.7% of DRPs. The number of patients with high-level medication adherence significantly increased from 17 to 28 after pharmacist-led education ($p < 0.001$). The number of seizures decreased in 19 patients (48.7%) during the 2-month period. Patient satisfaction was high in all patients.

Conclusion: It is shown that the contribution of pharmacists in treating patients with epilepsy is beneficial in improving medication adherence, detection and management of DRPs, and decreasing the number of seizures.

Key words: Drug-related problems, epilepsy, medication adherence, patient education, pharmacist

INTRODUCTION

Epilepsy, one of the most common neurological illnesses worldwide and with neurobiological, cognitive, psychological, and social consequences, is a chronic neurological disorder characterized by recurrent and unprovoked seizures that frequently begin in childhood or adolescence.[1,2] Therefore, epilepsy may lead to an increase in morbidity and restriction of daily activities and occupational abilities.[3] The lack of seizure control has unfavorable outcomes such as falls, injury, increased admission rate in physician office hospitalization, loss of work, and increase in healthcare cost.[4]

Antiseizure drugs (ASMs) are the principal treatment options for controlling or preventing seizures in patients with epilepsy.[5] Although appropriate use of ASMs reduces the frequency of seizures by approximately 67%, epilepsy can remain unrestrained in some patients.[5,6] However, in 70-80% of patients with new-onset epilepsy, seizures can be entirely controlled with appropriate ASM choice and medication adherence.[1] Medication adherence refers to the extent to which the recommendations given by a healthcare professional are followed by the patient. Ensuring medication adherence is important in terms of contributing to the drug selection of patients and strengthening the relationship between the healthcare provider and the patient.[7] Drug-specific adherence problems in patients with epilepsy are considered the high frequency of ASMs, polytherapy, and ASM-specific problems

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such as adverse events and low efficacy.[8] Additionally, ASMs have serious adverse effects that may lead to discontinuation of drug therapy, non-adherence, and a negative impact on the quality of life of patients with epilepsy. Therefore, optimization of treatment must ensure the safety and efficacy of ASMs.[9]

Another concern is comorbidities and co-medications with ASMs, which may enhance the frequency of drug-related problems (DRPs) and drug-drug interactions that may lead to loss of seizure control, adverse effects, and toxicity.[10] Clinical pharmacists have many significant roles in this patient group, such as therapeutic drug monitoring, interpretation of laboratory tests, determination of drug-drug interactions and adverse effects of medications, dosage adjustment, and patient education regarding medications and diseases.[11] A systematic review emphasized that clinical pharmacists may have a positive impact on medication adherence, patients' knowledge regarding medications and disease, and the quality of life of patients with epilepsy.[12] In a study, it was revealed that adherence improvement education and motivational interviews provided by the pharmacist reduced the number of seizures and improved ASM knowledge in patients with epilepsy.[13] DRPs contribute to non-adherence or low adherence rates due to inappropriate medication use and adverse effects.[14] Because medication adherence is essential to ensure the control of seizures and prevent treatment failure, pharmacist-led educational interventions may be beneficial in the management of epilepsy. In this study, we detected and manage DRPs, reduce the number of seizures, and improve medication adherence through pharmacist-led education in patients with epilepsy.

MATERIALS AND METHODS

Study design

This study was an interventional, pre-post, collaborative, and prospective study with 2 months a 2-month patient follow-up period.

Study settings

This study was conducted at the University of Health Sciences, Türkiye, Izmir Tepecik Training and Research Hospital between April 15 and October 31, 2019, in Türkiye. The hospital has a rational drug usage unit that belongs to the hospital pharmacy. This study was conducted in collaboration with the rational drug usage unit and the Department of Neurology.

Study population

All patients over 18 years-old with epilepsy, who were able to communicate, used more than four medications and were willing to sign an informed consent form were involved in the study. Patients who have cognitive impairment (such as dementia, Alzheimer's disease), speech disorder, pregnancy or decline to participate in our study were excluded.

Routinely, patients admitted to the Neurology Outpatient Clinic receive epilepsy care from the physician. Following the physician-patient interview, patients who meet the inclusion criteria are directed to the rational drug use unit by the physician. Within the scope of this study, detection and treatment of DRPs and education on disease, medication, and lifestyle changes were provided to patients by the pharmacist in the rational drug unit.

Data collection

During the first interview, the patient's demographics, routine medications, herbal medications, comorbidities, number of ASMs, and number of seizures were recorded in patient follow-up forms from the hospital information system database and patients through a face-to-face interview. To determine DRPs, the Pharmaceutical Care Network Europe (PCNE 8.01) classification was performed by the pharmacist. The pharmacist reported the interventions to the physician to resolve the identified DRPs. Additionally, we used the Morisky-Green-Levine Scale (MGLS) to assess medication adherence. After two months, when patients visited their physicians for routine follow-up, a second patient-pharmacist interview was conducted. During the second interview, MGLS and the Patient Satisfaction with Pharmacist Services Questionnaire (PSPSQ 2.0) were administered, and the number of seizures within those two months was recorded.

Tools

In the first pharmacist-patient interview, the pharmacist applied the MGLS to assess the medication adherence level. Self-reporting medication adherence scales have many advantages, such as being cost-effective, brief, patient-centered, and having good psychometric properties. Developed by Donald E. Morisky and validated by Morisky, Green, and Levine, self-reporting MGLS, which consists of 4 "yes" (0 point) and "no" (1 point) questions, is used to evaluate the medication adherence of patients with chronic diseases. The medication adherence level of patients. This study's aimedents were determined as low (0 point), medium (1-2 points), and high (3-4 points). The validity of the MGLS was validated and translated into Turkish by Yilmaz and Buzlu.[15]

PCNE classification is an instrument that is periodically updated and widely used for the classification of DRPs. In our study, PCNE was used to classify pharmacist-identified DRPs and their causes, interventions, and outcomes. PCNE version 8.01 consists of 5 main domains (P: Problems; C: Causes; I: Planned intervention; A: Acceptance; O: Status of acceptance).[16]

Developed by Sakharkar et al.[17] PSPSQ 2.0 is an instrument for evaluating the satisfaction of patients with chronic diseases in pharmaceutical services. PSPSQ comprises 22 questions, and each question is scored on a 4-point Likert scale (strongly agree, agree, disagree, and strongly disagree) ranging from 1 to 4 points. In addition, three sub-dimensions (quality of care, patient-pharmacist relationship, and overall satisfaction) are involved in the PSPSQ. The study of validation and translation into Turkish was conducted by Okuyan et al.[18] The translated form of the PSPSQ consists of 20 questions, excluding the 5th and 19th questions.

Interventions

A pharmacist-led education service was provided to patients during the face-to-face pharmacist-patient interview.

Educational interventions were determined by the physician and pharmacist. Educational interventions increase medication adherence. In this context, following the determination of the patient's medication usage pattern, the importance of medication adherence, non-adherence, and its leading to problems were learning objectives. To identify DRPs, we used patient and hospital information database notes. The pharmacist asked questions about prescribed or over-the-counter medicines, herbal drugs, and adverse effects during the patient-pharmacist interview. Additionally, drug interaction assessment was performed using web tools. If the pharmacist determined a DRP, it was classified according to PCNE. Following this process, pharmacist interventions were proposed to the physician or patients. While for the interventions at the prescriber level, the acceptance rate of interventions and status of DRPs were assessed in the first interview, for the interventions at the patient level, the acceptance rate and status of DRPs were assessed in the second interview.

Statistical analysis

Quantitative variables were described using means, standard deviations (SD), medians (minimum-maximum), and frequencies (percentage) for categorical variables. The Wilcoxon test was used to evaluate the differences in the DRP rate before and after pharmacist-led education. The significance level was defined as $p < 0.05$. SPSS version 25.0 was used to perform all statistical analyses (IBM Corporation, New York, USA).

Ethical approval

The study was approved by the University of Health Sciences Türkiye, Izmir Tepecik Training and Research Hospital Non-Interventional Research Ethics Committee (no: 2019/6-10).

RESULTS

The data from 39 patients with epilepsy (56.4% male) who met the inclusion criteria were analyzed in this study. During the study period, 78 interviews were conducted with the pharmacist. The mean (± SD) age of patients was found 43.6 ± 12.6 years. Most of the patients stated no alcohol consumption, no herbal supplement or non-prescription medication use, and no ability to manage self-care (89.7%, 76.9%, and 79.5%, respectively). The most common comorbidities were major depression (25.6%), hypertension (18%), and hypothyroidism (10.3%). The mean number of drugs *per* patient was 5.5 ± 1.1 and the mean number of ASMs was 2.7 ± 1.0. In addition, the most used ASMs were sodium valproate (71.1%), carbamazepine (56.4%), levetiracetam (38.6%), and lamotrigine (38.6%). The clinical characteristics of the patients are shown in Table 1.

Medication adherence was found to be moderate in 21 patients (53.9%) at baseline, and a significant increase in medication adherence was observed after pharmacist-led education, and the number of patients with high-level medication adherence increased from 17 to 28 ($p < 0.001$) (Table 2). When the influence of education level on medication adherence was evaluated, the number of patients with high-level medication adherence increased after education both in primary school (from 6 patients to 17 patients) and high school (from 9 patients to 11 patients) graduates ($p < 0.001$).

The number of seizures decreased in 19 patients (48.7%), increased in 3 patients (7.7%), and did not change in 17 patients (43.6%) during the 2-month period before and after pharmacist-led education. All patients were satisfied with the pharmacist's service (PSPSQ 2.0; disagree 0%, strongly disagree 0%). Higher satisfaction among patients was detected according to each part of PSPSQ 2.0 (quality of care, patient-pharmacist relationship, overall satisfaction) at the end of the study (Table 3).

A total of 59 DRPs (1.5 DRPs per patient) were detected during the study period (Table 4). The majority of DRPs were associated with treatment safety based on the adverse drug reactions of ASMs. Patient-related DRP causes were associated with inappropriate drug use. The majority of

Table 1. Clinical characteristics of patients (n: 39)

	n (%)
Gender	
Women	17 (43.6)
Men	22 (56.4)
Education	
Illiterate	4 (10.3)
Primary school	23 (59.0)
High school	12 (30.8)
Comorbidity	
No comorbidity	17 (43.5)
1	18 (46.2)
2	4 (10.3)
Number of anti-seizure drugs	
1	5 (12.8)
2	9 (23.1)
3	18 (46.2)
4	5 (12.8)
5	2 (5.1)

Table 2. Medication the medication adherence level according to MGLS before and after education (n: 39)

	Before education	After education	
Medication adherence, MGLS	**n (%)**	**n (%)**	***p***
Low	1 (2.6)	1 (2.6)	
Moderate	21 (53.9)	10 (25.6)	<0.001
High	17 (43.6)	28 (71.8)	

MGLS: Morisky-Green-Levine scale, statistical analysis: Wilcoxon

Table 3. Pharmacist service satisfaction of patients according to PSPSQ 2.0 (n: 39)

	Strongly agree	Agree	Disagree	Strongly disagree
	n (%)			
Quality of care	11 (28.6%)	28 (71.4%)	0 (0%)	0 (0%)
Patient-pharmacist relationship	17 (44.5%)	22 (55.5%)	0 (0%)	0 (0%)
Overall satisfaction	33 (85.5%)	6 (14.5%)	0 (0%)	0 (0%)

PSPSQ 2.0: Patient Satisfaction with Pharmacist Services Questionnaire-Version 2.0

Table 4. DRPs according to PCNE 8.01 classification (n: 59)

Domains			
Problems (P)	**Code**	**Definitions**	**n (%)**
Treatment effectiveness	P1.2	Effect of drug treatment not optimal	12 (20.3)
	P1.3	Untreated symptoms or indications	8 (13.6)
Treatment safety	P2.1	Adverse drug event (possibly) is occurring	31 (52.5)
Others	P3.2	Unnecessary drug-treatment	5 (8.5)
	P3.3	Unclear problem/complaint	3 (5.1)
Causes (C)	**Code**	**Definitions**	**n (%)**
Drug selection	C1.4	Inappropriate combination of drugs or drugs and herbal medication	3 (5.1)
Dispensing	C5.1	Prescribed drug not available	2 (3.4)
	C5.2	Necessary information not provided	1 (1.7)
Drug use process	C6.1	Inappropriate timing of administration and/or dosing intervals	7 (11.9)
	C6.2	Drug under-administered	1 (1.7)
The patient related	C7.1	Patient uses/takes less drug than prescribed or does not take the drug at all	8 (13.6)
	C7.2	Patient uses/takes more drug than prescribed	1 (1.7)
	C7.4	The patient uses unnecessary drugs	4 (6.8)
	C7.5	The patient takes food that interacts	4 (6.8)
	C7.7	Inappropriate timing or dosing intervals	1 (1.7)
	C7.8	Patient administers/uses the drug in the wrong way	22 (37.3)
	C7.9	Patient unable to use the drug/form as directed	3 (5.1)
Other	C8.1	No or inappropriate outcome monitoring	2 (3.4)
Planned interventions	**Code**	**Definitions**	**n (%)**
At the prescriber level	I1.3	Intervention proposed to the prescriber	2 (3.4)
	I1.4	Intervention discussed with the prescriber	13 (22.0)
At the patient level	I2.1	Patient (drug) counseling	37 (62.7)
	I2.4	Spoken to a family member orcaregiver	1 (1.7)
At the drug level	I3.4	Instructions for use changed to ...	4 (6.8)
	I3.5	Drug stopped	1 (1.7)
Other intervention or activity	I4.1	Other intervention (specify)	1 (1.7)

Table 4. Continued

Intervention acceptance	Code	Definitions	n (%)
Intervention accepted (by prescriber or patient)	A1.1	Intervention accepted and fully implemented	42 (71.2)
	A1.2	Intervention accepted, partially implemented	11 (18.6)
	A1.3	Intervention accepted but not implemented	4 (6.8)
	A1.4	Intervention accepted, implementation unknown	1 (1.7)
Other (no information on acceptance)	A3.1	Intervention proposed, acceptance unknown	1 (1.7)
Status of the DRP	**Code**	**Definitons**	**n (%)**
Not known	O0.1	Problem status unknown	3 (5.1)
Solved	O1.1	Problem solved	37 (62.7)
Partially solved	O2.1	Problem partially solved	14 (23.7)
Not solved	O3.1	Problem not solved, lack of cooperation of patient	5 (8.5)

DRPs: Drug-related problems, PCNE 8.01: Pharmaceutical Care Network Europe, version 8.01

pharmacist interventions was at the patient level such as patient counseling, especially on drug use (62.7%). Most of the interventions (71.2%) were accepted and implemented by both physicians and patients, and 62.7% of DRPs were completely solved *via* pharmacist interventions.

DISCUSSION

The fundamental components of epilepsy therapy are seizure control and DRP minimization. The emergence of DRPs in routine practice, however, is an unavoidable undesirable circumstance. Furthermore, DRPs contribute to lower medication adherence, quality of life, and treatment satisfaction. In this study, DRPs and the impact of pharmacist-led education on medication adherence rates were assessed in 39 patients with epilepsy. We found that the education provided by pharmacists positively affected the medication adherence rate and solved most DRPs.

Medication adherence requires ensuring optimal pharmacotherapy to prevent treatment failures in patients with epilepsy. In addition, pharmacists play a key role in ensuring medication adherence through educational methods and pharmaceutical care. The baseline ASM adherence rate was found 43.6%, slightly lower than other studies in Ethiopia (55.7%) and China (51.9%).[10,19] Patient characteristics (cultural, socio-demographic, and education levels, *etc.*), study methods and tools used to measure medication adherence may have caused this discrepancy. Medication adherence can be assessed in a variety of ways, including pill counting, therapeutic drug monitoring, and electronic tools, although there is no gold standard. In our study, medication adherence was measured using a self-report tool; however, the use of an additional method to assess medication adherence could have supported the results.

Many studies display the positive impact of pharmacists on medication adherence. Consistent with previous studies, our study showed that medication adherence was positively affected by pharmacist-provided educational interventions.[13] In addition, the differences in education level among patients with epilepsy may have influenced the difference in the effect of pharmacist-led education on medication adherence. Similar to our findings, higher medication adherence was detected in patients with higher educational levels compared with patients with lower educational levels in a recent study.[7] Therefore, in particular high educational status patients, pharmacist-led educational interventions may be more beneficial to improve medication adherence. Ensuring optimal medication adherence may play an important role in reducing the frequency of seizures. A positive correlation between poor medication adherence and more seizures has been found in recent studies.[3,20] Similar to the literature, the frequency of seizures was also decreased in our study because of increased medication adherence with pharmacist-led education.

DRPs are an obstacle to ensuring optimal drug therapy and high medication adherence and preventing seizures. The detection and solution of DRPs play an important role in managing the treatment appropriately. In our study, it was found that DRPs *per* patient were 1.5 on treatment effectiveness. In a study, it was found that the DRP of patients admitted to the rheumatology and internal diseases outpatient clinic was 2.4 *per* patient, and 63% of DRPs were clinically significant.[21] This discrepancy may be explained by the use of more drugs in rheumatology and internal disease, the high number of patients, and the high incidence of possible drug-drug interactions. Additionally, solutions to DRPs must be conducted together with patients and health care professionals. From the results of our study, most DRPs were solved by pharmacist intervention, consistent with a study.[22] The safety of ASMs plays a key role in maintaining treatment and preventing problems of other existing comorbidities. In a previous study, optimal ASM treatment of patients with epilepsy at a nursing home was challenged by adverse effects and drug-drug interactions.[23] Findings from our study, treatment safety (possible adverse effects) and treatment effectiveness problems were found to be major problems. Drug-drug interactions were not clinically significant, and this may be explained by the existence of relatively young patients and the low incidence of polypharmacy in our study. The major cause of detected

DRPs was patient-related problems (inappropriate drug use by patients); therefore, planned intervention was provided at the patient level in our study. In addition, the pharmacist's interventions and recommendations regarding the management of DRPs are highly accepted by physicians. In our study, most of the interventions were at the patient level, but as consistent with other studies, intervention at the prescriber level was highly accepted and applied.[21,24]

Patient satisfaction with pharmacy services may be positively affected by pharmacist-led education in patients with chronic diseases such as epilepsy. Similar to our findings, the satisfaction of patients with chronic disease was found to be high in other studies as well.[18] In a brief communication, it was shown that patient satisfaction was improved by ensuring high medication adherence in patients with epilepsy.[25]

Study limitations

This study has some limitations. The number of patients was limited because of the short study period and the distance between the locations of the neurology department and the rational drug usage unit. In addition, because of the involvement of younger patients, fewer comorbidities, and less drug use, the determination of DRPs was limited.

CONCLUSION

In conclusion, the pharmacist in the multidisciplinary team has key roles such as ensuring medication adherence, detection and management of DRPs, and contributing to optimal treatment during the follow-up period of patients with epilepsy. Because of high patient satisfaction and improved medication adherence, pharmacist-led education plays an important role in ensuring optimum therapy.

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Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences, Türkiye, Izmir Tepecik Training and Research Hospital Non-Interventional Research Ethics Committee (no: 2019/6-10).

Informed Consent: All participants involved in this study signed the informed consent form.

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Authorship Contributions

Surgical and Medical Practices: E.Ö., A.Ç.T., İ.F.U., Concept: E.Ö., K.D., Design: E.Ö., A.Ç.T., İ.F.U., U.Ş., K.D., Data Collection or Processing: E.Ö., Analysis or Interpretation: E.Ö., K.D., U.Ş., Literature Search: O.F., E.Ö., Writing: O.F., E.Ö.

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