International Journal of Basic & Clinical Pharmacology
Joshi KP et al. Int J Basic Clin Pharmacol. 2023 Jul;12(4):563-569
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20231892

Original Research Article

A cross-sectional questionnaire-based study of medication adherence in children suffering from epilepsy attending pediatric out-patient department at a tertiary care teaching hospital

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Received: 03 May 2023
Accepted: 31 May 2023

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ABSTRACT

Background: Epilepsy is a common chronic disease presenting during childhood that requires long-term treatment. Rates of adherence to antiepileptic drugs are variable in children ranging from 25% to 75%. Non-adherent patients are more likely to experience frequent and recurrent seizures which drastically impact the health of the patient. This study was therefore conducted in order to assess the medication adherence of children suffering from epilepsy to the prescribed anti-epileptic drug therapy.
Methods: Children diagnosed with epilepsy aged 6-18 years were enrolled in the present cross-sectional questionnaire-based study after prior written informed consent and written informed assent. Children with co-morbidities were excluded from the study (as diagnosed by the Paediatrician). The case record form was filled after interviewing the patients. A questionnaire based on the Morisky medication adherence scale-8 (MMAS) was used to evaluate the quality of life of children.
Results: Total 243 patients got enrolled in the study. GTCS was found to be the most common type of epilepsy. Valproate was the most commonly used agent. Out of the 243 patients in total, 201 patients (83%) showed high adherence, 24 patients (10%) showed medium adherence and 18 patients (7%) showed poor adherence to the treatment prescribed. Patients on monotherapy showed higher adherence rates than patients on polytherapy. Medication adherence was highest with Valproate among monotherapy and valproate + carbamazepine among poly-therapy.
Conclusions: We conclude that monotherapy with anti-epileptic agents and patient satisfaction is positive predictors of medication adherence leading to a lesser impact of the disease on the child and improved health.

Keywords: Cross-sectional study, Epilepsy, Medication adherence, Pediatric

INTRODUCTION

Epilepsy is a chronic disorder characterized by recurrent unprovoked seizures which affect people of all ages.[1] It is a common chronic neurological condition in developing years of a child's life that can negatively impact a child's physical, social, cognitive, psychological and emotional function.[2,3]

WHO defines adherence to long-term therapy as "the extent to which, a person's behaviour taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider".

Several systematic reviews have found that in developed countries, medication adherence among patients suffering from chronic diseases averages only about 50%. The

magnitude and impact of poor adherence in developing countries is assumed to be even higher owing to the comparative lack of health resources and lesser access to healthcare facilities. There is strong evidence that many patients with chronic diseases find it difficult to adhere to their recommended regimens. It causes medical as well as psychosocial complications of the disease, reduces patients' quality of life and wastes health care resources.[4] Rates of adherence to antiepileptic drugs are variable in children ranging from 25% to 75%.[5] Non-adherent patients are more likely to experience frequent and recurrent seizures which drastically impact the health of the patient.

One of the most frequently used patient questionnaires for the assessment of medication adherence is the MMAS. The tool uses a series of short behavioural questions prepared in such a way as to avoid "yes-saying" bias which is commonly seen with patients suffering from chronic diseases. More specifically, the wording of the questions is arranged in a way to prevent answers that tend to follow certain behavioural patterns. This allows the patient to respond to questions about non-adherence in a spirit of full disclosure for the clinician and reduces the chances of bias.[6]

This study was planned to reveal the promising impact of adherence to antiepileptic drug therapy on the lives of children. This study addressed the medication adherence of children suffering from epilepsy to the prescribed anti-epileptic drug therapy.

Aim and objective

Aim and objectives were to analyze medication adherence score in children suffering from epilepsy, to evaluate association between anti-epileptic drug used and medication adherence.

METHODS

The study carried out at the pediatrics out-patient department, SSG hospital, Vadodara is a hospital-based cross-sectional observational study conducted over a period of 9 months, from November 2021 to July 2022. It is a questionnaire-based study in children diagnosed with epilepsy aged 6 to 18 years.

Inclusion criteria

Children (6-18 years of age) suffering from only epilepsy for at least one month, children whose parents give consent to participate in the study, children who give assent to participate in study were included in the study.

Exclusion criteria

The children with other co-morbid conditions as diagnosed by the paediatrician were excluded.

Before obtaining the required information: (1) Prior written informed consent of the parent/LAR was taken. (2) For children between 6 and 12 years of age, oral assent was obtained in the presence of parent/LAR. (3) For children between 12 and 18 years of age, written assent was obtained. The patient information sheet, informed consent form and informed assent form were all translated to vernacular languages i.e., Hindi and Gujarati.

All children suffering from epilepsy and/or their parents were subjected to the questionnaire after a thorough explanation, written informed consent and oral/written informed assent. The questionnaire consisted of two parts: The first part contained relevant demographic and detailed medical history including drugs prescribed, their dosage forms, route of administration, frequency of administration and duration of therapy. The second part contained a questionnaire for medication adherence based on MMAS-8. Confidentiality and data safety was maintained throughout the process.

Data from all the patients who fulfilled the inclusion and exclusion criteria was recorded in the case record form. This included demographic characteristics of the patients, diagnosis of the present condition, significant present and past medical history and detailed treatment history. Descriptive analysis was done from the obtained data. The recorded data was entered in an excel spreadsheet and analyzed for percentage and frequency.

RESULT

A total of 243 patients were enrolled in the study, of which n=32 patients belonged to the age of 10 years (13.16%), followed by 9 years (n=30, 12.32%). The least number of patients belonged to the age of 18 years (n=2, 0.82%). Amongst the 243 patients, 163 (67%) were male and 80 (33%) were female (Figure 1).

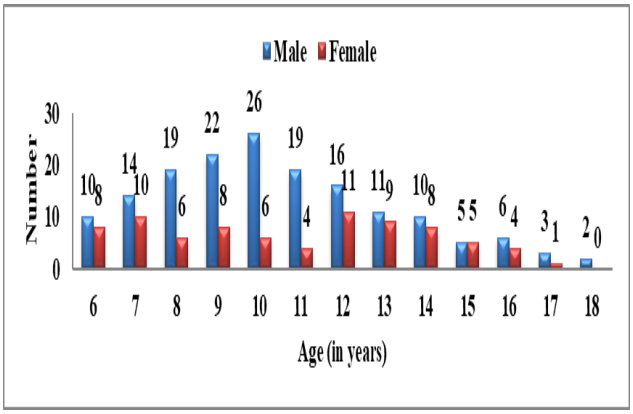

Figure 1: Age and gender wise distribution of patients.

Types of seizures

The most common type of seizure found was generalized tonic-clonic seizure (n=149, 61%), followed by focal seizure (n=47, 19%), myoclonic and clonic seizures (n=20,

8%), atonic seizure (n=6, 3%) and absence seizure (n=1, 0.4%) (Table 1).

Table 1: Types of seizures.

Type of seizure	N	Percentage (%)
Generalized tonic-clonic seizure	149	61.31
Focal seizure	47	19.34
Myoclonic	20	8.23
Clonic seizure	20	8.23
Atonic seizure	6	2.46
Absence seizure	1	0.41
Total	243	

Drugs prescribed

The most common antiepileptic agent prescribed was Valproate (n=174, 39%) followed by Carbamazepine (n=61, 13%), Levetiracetam (n=30, 7%) and Clobazam (n=8, 2%). Other drugs prescribed were MVBC, Folic acid and Calcium + vitamin d_3, accounting for (n=345, 56%) of prescriptions (Table 2).

Table 2: Drugs prescribed.

Drug	N
Valproate	174
Carbamazepine	61
Levetiracetam	30
Clobazam	8
Others (MVBC, FA, Calcium + vit D_3)	345
Total	618

Polytherapy vs monotherapy (Anti-epileptic agents)

Monotherapy observed to be more common (n=213, 88%) as compared to polytherapy (n=30, 12%) (Figure 2).

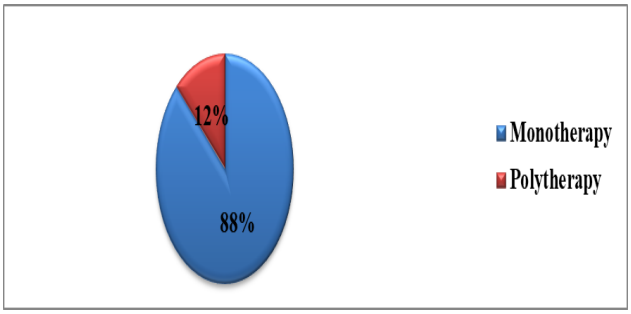

Figure 2: Polytherapy vs monotherapy (Anti-epileptic agents).

Anti-epileptic agents prescribed as polytherapy

The most common drugs prescribed together were Carbamazepine + Valproate (n=16, 53%). Valproate + Clobazam (n=8, 27%), Carbamazepine + Levetiracetam (n=5, 17%) and Valproate + Levetiracetam (n=1, 3%) were the other combinations prescribed (Table 3).

Table 3: Anti-epileptic agents prescribed as polytherapy.

Antiepileptic agents prescribed as polytherapy	N	Percentage (%)
Carbamazepine + Valproate	16	53.33
Valproate + Clobazam	8	26.66
Carbamazepine + Levetiracetam	5	16.66
Valproate + Levetiracetam	1	3.33
Total	30	

Other drugs prescribed

Amongst the other drugs prescribed, MVBC was prescribed n=42 times (24%), MVBC + FA was prescribed n=45 times (25%), MVBC + calcium/vit D_3 was prescribed n=54 times (31%) and MVBC + FA + Calcium/Vit D_3 were prescribed n=35 times (20%) (Table 4).

Table 4: Other drugs prescribed.

Other drugs prescribed	N	Percentage (%)
MVBC alone	42	12.17
MVBC + Folic acid	45	13.04
MVBC + Calcium/ vit D_3	54	15.65
MVBV + FA + Calcium/Vit D_3	35	10.14
Total	176	

Medication adherence of patients

Out of the 243 patients in total, 201 patients (83%) showed high adherence, 24 patients (10%) showed medium adherence and 18 patients (7%) showed poor adherence to the treatment prescribed (Figure 3).

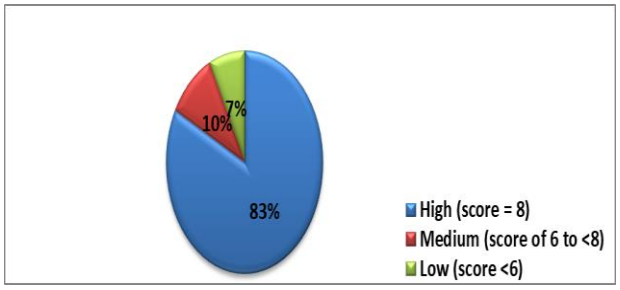

Figure 3: Medication Adherence of patients.

Medication adherence to anti-epileptic agents

Amongst the 149 patients who were prescribed Valproate alone, 132 patients (89%) revealed having high adherence,

12 patients (8%) revealed having medium adherence and 5 patients (3%) revealed having poor adherence to the treatment prescribed (Figure 4).

From the 16 patients prescribed valproate + Carbamazepine, 14 patients (87%) were found to have high adherence and 2 patients (13%) were found to have poor adherence to the treatment prescribed (Figure 4).

A total of 8 patients were prescribed Valproate + Clobazam, of which 6 patients (75%) were observed to have high adherence and 1 patient each had medium adherence (12%) and poor adherence (12%) to the treatment prescribed (Figure 4).

The patient prescribed Valproate + Levetiracetam had shown poor adherence to the treatment prescribed.

There were 40 patients who were prescribed Carbamazepine alone, of which 30 patients (75%) had high adherence, 6 patients (15%) had medium adherence and 4 patients (10%) had poor adherence to the treatment prescribed (Figure 4).

The 5 patients who were prescribed Carbamazepine + Levetiracetam, revealed high adherence in 3 patients (60%), medium adherence and poor adherence in 1 patient each (20% each) (Figure 4).

Among the 24 patients prescribed Levetiracetam alone, 16 patients (67%) were observed to have high adherence, 4 patients (16%) %) were observed to have medium adherence and 4 patients (17%) were observed to have poor adherence to the treatment prescribed (Figure 4).

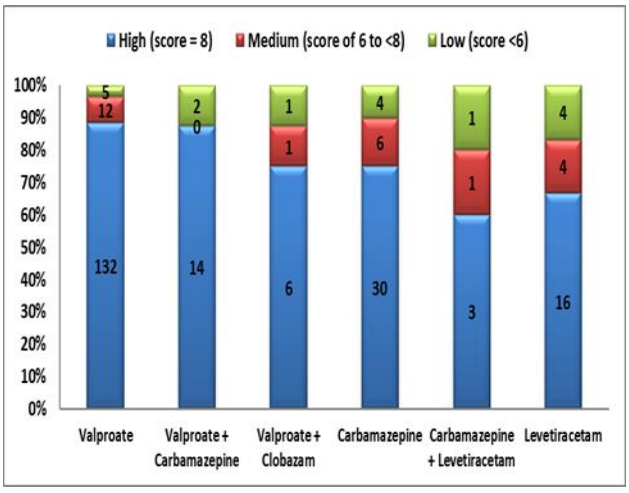

Figure 4: Medication adherence to anti-epileptic agents.

DISCUSSION

Epilepsy is a chronic and serious neurological disorder with multifaceted uncertainties and stigmatization which have a significant negative role in lives of those affected by the disease.[7] It may interfere with social functioning by limiting educational opportunities, employability, interpersonal relationships and also increase the risk of death.[8]

Pediatric patients are anatomically and physiologically different from normal healthy adults in various aspects. The physiological systems are also in a growing phase that contributes to differences in the rate and extent of drug absorption, metabolism, excretion (pharmacokinetics) as well as pharmacodynamic effect as compared to a normal healthy adult.[9]

Several studies indicate that childhood epilepsy is a high-risk factor for poor psychosocial outcomes, including depression, anxiety, low self-esteem, behavioural problems and academic challenges.[10] The management of epilepsy has traditionally focused on seizure control and reduction in seizure frequency as the main goals for successful treatment.

A total of 243 patients were enrolled in the study, out of which most of the patients belonged to the age of 10 years (13.16%) and 9 years (12.32%), followed by 12 years (11.11%). The least number of patients belonged to the age of 18 years (0.82%). Amongst the 243 patients, 163 (67%) were male and 80 (33%) were female.

The most common type of seizures observed were generalized tonic-clonic seizures (n=149, 61%), followed by focal seizures (n=47, 19%), myoclonic and clonic seizures (n=20, 8%). This was similar to the one observed by Malhi et al and Chauhan et al.[11,12]

Sodium valproate was the most commonly prescribed antiepileptic agent (n=174, 28%) followed by Carbamazepine (n=61, 10%), Levetiracetam (n=30, 5%) and Clobazam (n=8, 1%), which was similar to study by Nagabushana et al and Chauhan et al. The observation of Valproate being the most commonly prescribed drug was also reported by Malhotra et al and Hasan et al.[3,12-14]

Monotherapy prescriptions (88%, n=213) were more common, similar to a study by Malhi et al, Nagesh et al and Chauhan et al. In a study by Sweileh et al polytherapy (64%) was more common than monotherapy (36%).[7,11,12,15]

Monotherapy should be tried before considering polytherapy. This is desirable because using a single drug controls seizure in most patients with fewer possible side effects. Monotherapy is preferred to polytherapy because of the lower medication cost, reduced potential for adverse reactions, undesirable drug interactions and improved medication adherence. This carries greater significance as our study population is children and adolescents.[13]

Amongst the other drugs prescribed, MVBC alone was prescribed n=42 (24%), MVBC + FA was prescribed n=45 (25%), MVBC + calcium/vit D_3 was prescribed n=54

(31%) and MVBC + FA + calcium/Vit D_3 were prescribed n=35 (20%).

There is strong evidence that many patients with chronic diseases find it difficult to adhere to their recommended regimens. Adherence is the degree to which a patient carries out the clinical recommendations of the treating physician.[16] Adherent behavior of a person with epilepsy can be defined as taking anti-epileptic agents on time and without fail, not manipulating their dosages, and following the physician's instructions regarding daily activities.[1] Medication adherence is regarded as a major challenge in developing countries.

Patients' nonadherent to medication can have many unwanted consequences such as poor control of the disease leading to an increase in clinic visits, hospitalizations, and also a decrease in productivity such as missing school and work.[17] Non-adherence may be the most important cause of poorly controlled epilepsy.[18]

To the best of our knowledge medication adherence among pediatric epileptic patients is scarcely reported from the Indian subcontinent.[12,19] The available studies have shown that in chronic illnesses (e.g., epilepsy, asthma and diabetes), patients have poor adherence ranging between 30%-70% as a result of lengthy duration of treatment, multiple medications, and remission of symptoms.[20-23] An adherence rate of greater than 95% may be needed to adequately suppress the epileptic seizures, thus missing a dose or two may suffice to cause failure of therapy and trigger seizures.[12,24] By improving medication adherence, epilepsy syndrome can be completely controlled and the number of seizures reduced in about 80% to 90% of the patients and these children can live, study and work like normal people as noted by Gao et al.[25]

Out of the 243 patients in total, 201 patients (83%) showed high adherence, 24 patients (10%) showed Medium Adherence and 18 patients (7%) showed poor adherence to the treatment prescribed. The pattern of medication adherence was found to be similar in a study by Qoul et al which showed an adherence rate of 79.5%.[23]

This was in contrast to a study by Malik et al in which the majority (58%) of patients were non-adherent to the treatment and in a study by Yang et al in which only 21.3% of the patients were found to be adherent to the prescribed treatment.[26,27] A similar observation was noted by Sweileh et al and Chauhan et al in which 64% and 70.54% of the patients were non-adherent to the prescribed treatment respectively.[12,15] This can be due to lesser overestimation of medication adherence, higher use of polytherapy or poorer patient education in these studies. Malik et al reported that polytherapy had a strong association with non-adherence, as 50% of the patients in the adherent group were on monotherapy as compared to 21% in the non-adherent group.[26] Their study illustrates the benefit of monotherapy with more patients showing medication adherence, which is essential for achieving seizure control compared with patients taking more than one anti-epileptic agent.[26] A similar trend was noted in our study with patients on monotherapy showing higher adherence rates than patients on polytherapy. It would therefore be beneficial to review patients on more than one Anti-epileptic Agent to ensure adherence and thus seizure control. In contrast, being on mono-therapy was described as a strong predictor of noncompliance in the research done by Buck et al.[28] This could be due to the fact that patients on polytherapy have a history of more frequent seizures and so come to feel it is more important to comply with their medication regime.

Among persons diagnosed with epilepsy, a majority will become free of seizures after appropriate treatment has been initiated. The maintenance of a seizure-free status necessitates continued antiepileptic therapy and avoidance of precipitating factors. Proper patient education by the health care professionals about the treatment regimen seems to play a vital role in increasing medication adherence among patients with chronic illness contributing to higher medication adherence rates in our study. A similar trend was also noted by Yang et al and Gopinath et al.[1,27] Malik et al noted that there was significance in the percentage of nonadherent children with epilepsy who reported receiving little or no counselling as compared to adherent children with epilepsy (86% vs 20% respectively) and in their study, adherent patients were significantly better counselled than non-adherent patients.[26] A significant factor that may lead to nonadherence is insufficient education regarding medication regimen and apprehension about adverse effects as pointed out by Gopinath et al.[1] They also reported that there was a significant negative correlation between poor doctor-patient communication and patient compliance. Chauhan et al observed that if patients are more satisfied with the treatment, then they are more likely to adhere to the medication regimen.[12]

Patients with epilepsy place great importance on having a doctor who is approachable, communicative and knowledgeable and on receiving adequate information about their condition. Patient satisfaction has been shown to influence health outcomes such as adherence to treatment and follow-up visits. Patients have been reported not to adhere to the advice given if they feel dissatisfied with a consultation. The patient's satisfaction with the consultation, his understanding and recall of the instructions and advice given can be used as a measure of the quality and effectiveness of doctor-patient communication.[1]

Our results suggest that healthcare providers should strongly emphasize medication adherence among their patients. Good lifestyle management is an important aspect of healthy living in patients with epilepsy, where medication adherence plays a pivotal role to have improved health.

Limitations

Being a cross-sectional study, it cannot predict the changes in medication adherence with time. This was a single-center study and hence the results cannot be extrapolated to other geographical areas and further studies need to be done to establish the generalizability of this study and determine the various factors that affect the medication adherence of children suffering from epilepsy. As the study is based on self-reports, it is prone to recall bias. Further, it is also possible that patients may have exaggerated their medication adherence. The patient with epilepsy might also have a memory deficit impacting their ability to recall and answer the questionnaire nearest to the truth.This study cannot exactly depict the prescription pattern of anti-epileptic medications due to low sample size.

CONCLUSION

The most common anti-epileptic agent prescribed was sodium valproate (n=174,39%). Monotherapy was observed to be more commonly prescribed (n=213, 88%) than polytherapy (n=30, 12%). The most common drugs prescribed together were carbamazepine + valproate (n=16, 53%). The degree of medication adherence was high in n=201 (83%), moderate in n=24 (10%) and low in n=18 (7%) patients. Monotherapy was found to be a positive predictor of high medication adherence.

ACKNOWLEDGEMENTS

Author would like to be thankful to the doctors and staff of paediatrics department for their support and help for identification of patients prescribed anti-epileptic agents.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Joshi KP, Bhave AL, Vyas PP. A cross-sectional questionnaire-based study of medication adherence in children suffering from epilepsy attending pediatric out-patient department at a tertiary care teaching hospital. Int J Basic Clin Pharmacol 2023;12:563-9.