




Prescribing Pattern and Medication Adherence in Patients with Epilepsy in a Tertiary Neuro-Center, Kathmandu

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Abstract

Background Epilepsy is a chronic condition characterized by unusual, frequent, excessive, and self-terminating neuronal firing. Adherence to medication is crucial to achieve the intended therapeutic outcome. However, not much research has been done on drug adherence in our context. Thus, the purpose of this study is to investigate the antiseizure medication prescribing pattern, medication adherence, and associated factors.

Materials and Methods A cross-sectional, analytical research was done on randomly selected epileptic patients through interview and documentary analysis using a semi-structured interview schedule and the eight-item Morisky Medication Adherence Scale (MMAS-8). The clinical and demographic characteristics were described using descriptive statistics (median, interquartile range [IQR], frequency, and percentage). The Shapiro–Wilk and chi-squared tests were used to examine the factors influencing medication adherence and the relationships between research variables. The analysis was performed using SPSS version 16.

Results From a total of 104 patients, 77.3% were males, the median age was 29 years (IQR: 16), the majority (42.3%) had higher secondary education, 15.4% had secondary education and 5.8% were illiterate, 25% were job holders, 26% were laborers, 41.3% were from province 3, and 16.3% were from province 4. Two-thirds (63.5%) of the patients were highly adherent to antiseizure medication and 54.8% were seizure free for more than 2 years.

The most common type of epilepsy diagnosed was generalized epilepsy (54.8%). Seizures were usually treated with monotherapy (65.4%), with sodium valproate being the most often used single antiseizure medicine (26.8%), followed by carbamazepine (16.3%) and levetiracetam (15.4%). Additionally, sodium valproate was the medication most frequently used in polytherapy for epilepsy. There was a strong association established between adherence and drug therapy type, age, adverse drug reaction, and

Keywords

- ▶ prescribing pattern
- ▶ medication adherence
- ▶ epilepsy
- ▶ antiseizure medication

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seizure control. The study revealed that adherence was not significantly associated with factors such as gender, occupation, regional distribution, or type of epilepsy.

Conclusion Low adherence was observed in 36.5% of patients. As a significant association was observed between medication adherence and seizure control, health care providers should focus on improving medication adherence. Evaluation of adherence needs to be a regular component of managing epilepsy. Further patients who do not stick to their drug regimens should receive more attention and assistance. It will support better therapy results.

Introduction

Recurrent episodic seizures, or at least two unprovoked (or reflex) seizures occurring more than 24 hours apart and affecting behavior, movement, sensations, or awareness, are the hallmarks of epilepsy, a neurological disorder.^{1–3} Usually, excessive and hypersynchronized brain neuron discharges are the cause.⁴ According to the International League Against Epilepsy (ILAE), epilepsies are classified into focal epilepsy, generalized epilepsy, and unknown epilepsy.^{3,5} The World Health Organization (WHO) estimates that there are 50 million people with epilepsy worldwide, 80% of whom live in developing countries. In Nepal, a nation with a population of 27.5 million people, roughly 30,000 people have sought treatment for seizure disorders, yet many Nepalese with epilepsy remain undiagnosed and untreated.⁶ The prevalence of epilepsy in Nepal is 7.3 per 1000 population.⁷ Social stigma and misunderstandings about the condition, as well as pervasive poverty, illiteracy, ineffective and unequally distributed health care systems, make it difficult to diagnose epilepsy and offer appropriate, affordable treatment.⁸ Medication adherence is essential for epileptics to avoid or minimize seizures and the overall impact they have on daily living.

In both developed and developing countries, nonadherence to medication remains a significant concern for health care providers as well as patients because of its adverse consequences on therapeutic outcomes. Unfortunately, data indicate that epilepsy patients' medication adherence is suboptimal.⁹ Numerous studies have revealed that a significant number of epileptic patients in low-resource nations never receive proper care for their illness, and many who are diagnosed and started on medication quickly discontinue it.¹⁰ According to a systematic review, the worldwide anti-seizure medication (ASM) nonadherence rate among patients with epilepsy was between 25 and 66%.^{11,12} Comparably, 34.1 to 65.4% of Ethiopians do not adhere to ASM.^{13,14} Similarly, poor adherence to ASM was reported in 64.1% of Malaysian epileptic patients, a larger percentage than in Western populations.¹⁵ The rate of medication adherence has been linked to several factors, such as age, gender, educational status, comorbidity, type of epilepsy, number of drugs, length of therapy, forgetfulness, and medication beliefs.^{13,14,16–19}

In the recent years, polypharmacy has increased tremendously in chronic diseases like epilepsy, so a prescription

pattern study will help identify the current practice of medications in epilepsy and its consequences.^{20,21} Drug use studies are effective tools in evaluating drug prescribing trends, efficiency, and cost-effectiveness of hospital formularies. Thus, the current study was conducted to determine the drug adherence of patients with epilepsy and to assess patterns of ASM usage in a tertiary neuro-center in Kathmandu.

Materials and Methods

Study Setting and Population

A cross-sectional study was conducted from December 2019 to January 2020 in the outpatient department of Upendra Devkota Memorial National Institute of Neurological and Allied Sciences (UDM-NINAS), Kathmandu, Nepal. Patients at least 18 years old who had been prescribed ASM within the previous 6 months were included in the study, excluding patients with new cases of epilepsy, pregnant/lactating women, and those patients who were physically and mentally incapable of giving consent.

Sample Size

The sample size was calculated using the Cochran formula $n = Z^2 pq/d^2$, where n = minimum sample size, Z = standard normal variate, p = estimated prevalence, $q = 1 - p$, d = desired level of precision or margin of error, and confidence interval = 95%. Therefore, Z -score = 1.96 and the estimated prevalence $p = 7.3\%$.⁷ Taking 95% confidence interval and 5% margin of error, the sample size was calculated as 104.

Data Collection and Variables

Data were collected by interviewing participants using a semi-structured questionnaire and the eight-item Morisky Medication Adherence Scale (MMAS-8), which was developed by Morisky et al.²² The tool was translated into the Nepali language by the researchers and was back-translated into English by a translator. Pretesting was done to ensure the appropriateness, reliability, and clarity of the questionnaire in 10% of the sample size. The individuals who participated in pretesting were not included in the study.

Dependent Variable

ASM nonadherence was measured with the validated MMAS-8. MMAS-8 comprises a total of eight questions that must be answered with yes or no. The scoring procedure

is as follows: for questions 1 to 4 and 6 to 7, each “no” answer receives a score of “1” and each “yes” receives a score of “0.” It is the opposite way around for question 5. On a 5-point Likert scale, the options for question 8 are the following: “never/rarely” (scored as 1), “once in a while” (scored as 0.75), “sometimes” (scored as 0.5), “usually” (scored as 0.25), and “all the time” (scored as 0). The total score of this questionnaire ranged from 8 to 0. Adherence to ASM was categorized into two categorical Likert scales: high adherence (6–8) and low adherence (<6). High and low adherence scores were calculated by using the mean adherence score.

Sociodemographic Variables

Sociodemographic variables included gender, age, education status, occupation, and state. Age was categorized into 18 to 25 years, 26 to 40 years, and above 40 years; education was categorized into illiterate, literate, secondary, higher secondary, and graduate; and occupation was categorized into farmer, service, business, teacher, laborer, students, unemployed, and others.

Statistical Analysis

Data were organized and stored in Microsoft Excel by using the validation command and analyzed in IBM SPSS version 16 software. Descriptive statistics (median, interquartile range, frequency, percentage) were used to describe the clinical and demographic variables. The determinants of medication adherence and the association between study variables were analyzed using a chi-squared test.

Results

Sociodemographic Characteristics

Out of 104 participants, the mean age of the participants was 31.9 ± 12.8 years (mean \pm standard deviation [SD]), ranging from a minimum of 18 to a maximum of 73 years. Out of the total participants, 70 (67.3%) were males and 34 (32.7%) were females. The educational background of the study participants was primarily higher secondary (42.3%), followed by graduate (24%), while 12.5% of the participants were literate and 5.8% were illiterate. Approximately 26% of the participants were literate and 5.8% were illiterate. Approximately 26% of the participants were laborer followed by 23.1% service, 18.3% farmers, 11.5% unemployed, 8.7% student, and 9.6% involved in other occupation (\rightarrow Table 1).

Clinical and Treatment Related Factors

Generalized epilepsy (54.8%) was identified in the majority of participants, followed by focal epilepsy (32.7%) and unknown epilepsy (12.5%). In all, 54.8% reported having no seizures for more than 2 years, but 74.1% reported experiencing side effects. For the treatment of generalized epilepsy, sodium valproate (34%) was the most frequently prescribed ASM, followed by levetiracetam (11%) and carbamazepine (9%). Of the responders, 65.4% were on monotherapy (\rightarrow Tables 2 and 3; \rightarrow Fig. 1).

Factors Associated with Medication Adherence

Compared with the 36.5% of patients who exhibited a low level of adherence, the MMAS-8 score showed that 63.5% of

Table 1 Sociodemographic characteristics of epileptic patients ($n = 104$)

| Variables | | Frequency | Percentage |
|--------------------|------------------|-----------|------------|
| Gender | Male | 70 | 67.3 |
| | Female | 34 | 32.7 |
| Age group | 18–25 y | 39 | 37.5 |
| | 26–40 y | 46 | 44.2 |
| | Above 40 y | 19 | 18.3 |
| Educational status | Illiterate | 6 | 5.8 |
| | Literate | 13 | 12.5 |
| | Secondary | 16 | 15.4 |
| | Higher secondary | 44 | 42.3 |
| | Graduate | 25 | 24.0 |
| Occupation | Farmer | 19 | 18.3 |
| | Service | 24 | 23.1 |
| | Business | 2 | 1.9 |
| | Teacher | 1 | 1.0 |
| | Laborer | 27 | 26.0 |
| | Student | 9 | 8.7 |
| | Unemployed | 12 | 11.5 |
| | Others | 10 | 9.6 |

Table 2 Distribution of patients with epilepsy by clinical related factors ($n = 104$)

| Variables | Category | Frequency | Percentage (%) |
|--------------------------|----------------------|-----------|----------------|
| Types of epilepsy | Focal epilepsy | 34 | 32.7 |
| | Generalized epilepsy | 57 | 54.8 |
| | Unknown epilepsy | 13 | 12.5 |
| Number of ASM prescribed | Monotherapy | 68 | 65.4 |
| | Polytherapy | 36 | 34.6 |
| Seizure-free period | Less than 2 y | 47 | 45.2 |
| | More than 2 y | 57 | 54.8 |
| Reported side effects | No | 27 | 25.9 |
| | Yes | 77 | 74.1 |

Abbreviation: ASM, antiseizure medication.

the patients demonstrated a high level of adherence. The Pearson chi-squared test was used to determine whether an association exists or not between the dependent and independent variables. The type of therapy, adverse drug reactions (ADRs), age group, and seizure-free years showed statistical significance with adherence; however, gender and epilepsy types did not show any significant association (\rightarrow Table 4).

Table 3 Distribution of patients with epilepsy by types of therapy (n = 104)

| Types of epilepsy | Types of therapy | | Frequency |
|----------------------|------------------|-------------|-----------|
| | Monotherapy | Polytherapy | |
| Focal epilepsy | 24 | 10 | 34 |
| Generalized epilepsy | 39 | 18 | 57 |
| Unknown epilepsy | 5 | 8 | 13 |

Discussion

Types of Epilepsy and Prescribing Pattern of Antiseizure Medication

Generalized epilepsy accounted for the majority of the patients' encounters with epilepsy (54.8%), with focal and unknown epilepsy following closely after. The current result differs with research conducted at Jimma University, Ethiopia (80%),²³ Bangladesh (74%),²⁴ India (55.22%),²⁵ multiple teaching hospitals in Pakistan (47%),²⁶ and Saudi Arabia (65%).²⁷ This difference could be attributed to variations in the level of competence and the diagnostic instruments employed, which aid in the classification of seizure types. Lack of proper classification of seizure types affects the selection of drugs and treatment outcome.²⁸

For managing generalized epilepsy, sodium valproate (34%) was the most commonly used single agent, followed by levetiracetam (11%) and carbamazepine (9%), while in treating symptomatic epilepsy, sodium valproate (32%) was the most commonly used single agent followed by carbamazepine (26%) and levetiracetam (21%). Findings from this study were consistent with those of other investigations, where phenytoin in India,⁹ valproate in Pakistan²⁶ and Saudi Arabia,²⁷ and carbamazepine in the United Kingdom²⁹ and Bangladesh²⁴ were mostly prescribed. Similarly, 65.4% of patients received ASM as monotherapy. The finding is in line with the study done in Jimma, Ethiopia (54.5%),²³ United Kingdom (95.7%),³⁰ India (62.4%),⁹ Cambodia (60%), Bangladesh (67%),²⁴ Pakistan (77.5%),²⁶ and Saudi Arabia (76.6%).²⁷ All these findings showed that treatment should be started with a single ASM (monotherapy) and the dose should be slowly built up until seizure control is achieved or side effects occur.

Similarly, in the present study, the most commonly prescribed ASM combinations were carbamazepine + clobazam (4.8%), levetiracetam + clobazam (3.8%), sodium valproate + phenytoin (2.9%), sodium valproate + clobazam (2.9%), sodium valproate + phenobarbital (1.9%), sodium valproate + lamotrigine + clobazam (3.8%), and carbamazepine + levetiracetam + clobazam (1.9%). This is in contrast to a study done by Tan et al in Singapore that observed sodium valproate + carbamazepine as the most common combination.³¹

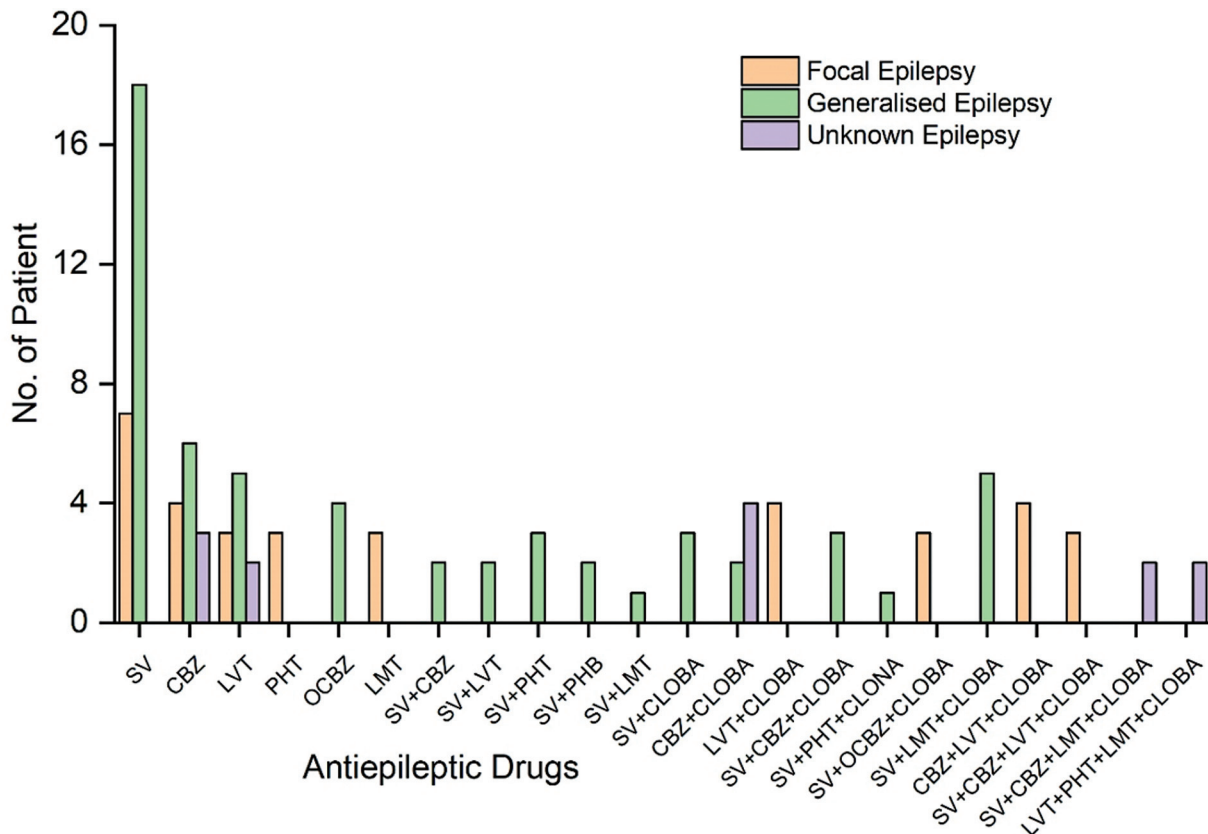


Fig. 1 Antiseizure medication utilization pattern among epileptic patients. Abbreviations: SV, Sodium valproate; CBZ, carbamazepine; LVT, levetiracetam; PHT, phenytoin; OCBZ, oxcarbazepine; LMT, lamotrigine; PHB, phenobarbital; CLOBA, clobazam; CLONA, clonazepam.

Table 4 Factors associated with medication adherence

| Variables | Subcategory | Low adherence, n (%) | High adherence, n (%) | p-value |
|--------------------|----------------------|----------------------|-----------------------|---------|
| Gender | Male | 25 (65.8) | 45 (68.2) | 0.802 |
| | Female | 13 (34.2) | 21 (31.8) | |
| Types of therapy | Monotherapy | 20 (52.6) | 48 (72.8) | 0.038 |
| | Polytherapy | 18 (47.4) | 18 (27.2) | |
| ADRs | Yes | 18 (47.4) | 9 (13.6) | 0.001 |
| | No | 20 (52.6) | 57 (86.4) | |
| Age group | 18–25 y | 13 (34.2) | 26 (39.4) | 0.025 |
| | 26–40 y | 13 (34.2) | 33 (50) | |
| | >40 y | 12 (31.6) | 7 (10.6) | |
| Types of epilepsy | Focal epilepsy | 11 (28.9) | 23 (34.8) | 0.340 |
| | Generalized epilepsy | 20 (52.6) | 37 (56.1) | |
| | Unknown epilepsy | 7 (18.4) | 6 (9.1) | |
| Seizure-free years | <2 | 32 (84.2) | 15 (22.7) | 0.001 |
| | >2 | 6 (15.8) | 51 (77.3) | |

Abbreviation: ADRs, adverse drug reactions.

Note: All p-values from a chi-squared test.

Factors Associated with Medication Adherence

One of the main problems with treating epilepsy is adherence to ASM. Poor adherence has received minimal attention in Nepal, despite being one of the primary reasons for nonresponsiveness to ASM therapy. Numerous methods can be used to assess adherence to ASM, such as self-reporting, pharmacy refill records, electronic monitoring, direct observation, and testing serum drug concentration.^{32,33} MMAS-8 was used in the present study and it showed that the majority (63.5%) of the patients in our study adhered to the prescribed ASM. A study conducted in St John's Medical College and Hospital,¹⁶ Neuro Spinal Hospital,³⁴ and France,³⁵ identified that 72.3, 70.8, and 79% of participants were adherent to the treatment. The high adherence in these studies might be because of the hospital-based participants who were more active, more health conscious, and hence were more motivated to adhere to their medication. However, the results were in contrast to another study that showed a low adherence.³⁶ The variations in the results could be attributed to the difference in data collection tools, the difference in sample size, or the true difference in different populations. Seizure-free year, age, and types of therapy and ADRs were observed to have significant associations with adherence. This finding is in line with the study that found a statistically significant association between the occurrence of ADRs and adherence. This could be because individuals who have negative side effects from their usual medications may decide not to take them regularly. However, a study done in the United Kingdom found that age does not affect the adherence of the patients.³⁷ This could be due to the difference in education level between the European community and the Nepalese community. In our study, we failed to find

any significant association between gender and types of epilepsy with ASM adherence.

Conclusion

In conclusion, among ASMs, sodium valproate was utilized as a monotherapy and a polytherapy, while the majority of other ASMs were recommended as add-on therapies. In all, 63.5% of patients were found to be adherent and 36.5% of the patients had low adherence. Drug therapy (monotherapy and polytherapy), ADRs, age, and seizure control have a significant effect on adherence. The sole limitation of the current study is that it was performed in a tertiary hospital, which made extrapolating our findings to a broader population challenging. We suggest that more research be conducted utilizing several recognized techniques to assess adherence in a more diverse group to further address the issue of ASM adherence in epileptic patients.

Ethical Consideration

Prior to data collection, permission was obtained from UDM-NINAS and the Institutional Review Committee at the Central Institute of Science and Technology, affiliated to Pokhara University, Nepal approved the study (Ref no.: IRC-02-076/077). Participants received a written consent form outlining all the facts in both Nepali and English. For illiterate individuals, inform consent was obtained by thumbprint after verbally giving the content provided in the form. They were informed that participation would be voluntary, and sufficient time was given to read and understand it. Any types of economic and other benefits were not provided and any influence was not used to collect the data from the patients.

Ethical Approval and Consent to Participate

Research was performed in accordance with the Declaration of Helsinki and was approved by the ethics committee Institutional Review Committee at Central Institute of Science and Technology (IRC-CiST), affiliated to Pokhara University, Nepal (Ref: IRC-02-076/077). All the patients gave written consent to participate in the study.

Authors' Contributions

S.T., P.P., and S.B.K. developed the study concept; S.T., P.P., and S.P. conducted the data mining and analysis; and P.P. and S.P. wrote the manuscript, which was reviewed and edited by all the authors.

Availability of Data and Materials

The dataset analyzed during the current study are available from the corresponding author on request.

Funding

None.

Conflict of Interest

None declared.

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