Factors Influencing Antiepileptic Drug (AED) Nonadherence in a Tertiary Care Hospital: A Cross-Sectional Study

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ABSTRACT

Introduction: Epilepsy affects almost 50 to 70 million individuals’ worldwide, accounting for 0.75 percent of the worldwide illness burden. Every year, an approximate of 2.4 million individuals are afflicted with epilepsy. Due to a lack of accessibility and affordability of AEDs, up to three-quarters of patients with epilepsy in low-income nations are unable to receive the medication they require.

Aim: To determine the factors influencing antiepileptic drug (AED) nonadherence in a tertiary care hospital.

Methodology: According to the findings of a single center, cross-sectional investigation, we did a subgroup assessment. Patients have to be at least 18 years old to participate. The Morisky Medication Adherence Scale, which has four items, was employed to assess compliance to AEDs. To forecast parameters linked to AED nonadherence, researchers employed multivariable logistic regression assessment.

Results: This subgroup evaluation includes a total of 270 patients who met the eligibility criteria. Amongst the patients, 82 (31%) did not take their medication as prescribed. AED polytherapy, medication linked negative events, and medication length beyond 3 years were three characteristics linked to poor adherence.

Conclusion: Almost one third of the participants did not take their medicine as prescribed. Noncompliance may be minimized if patients’ treatments are limited to monotherapy as much as feasible and patients are taught about the length of medication and potential side effects of AEDs.

Key Words: Epilepsy, Antiepileptic dugs, Compliance, Poly therapy, Potential side effects, Morisky Medication Adherence Scale

INTRODUCTION

Epilepsy affects almost 50 to 70 million individuals’ worldwide, accounting for 0.75 percent of the worldwide illness burden.¹ ² ³ Every year, an approximate of 2.4 million individuals are afflicted with epilepsy. Due to a lack of accessibility and affordability of AEDs, up to three-quarters of patients with epilepsy in low-income nations are unable to receive the medication they require. ⁴ With presently accessible antiepileptic medicines, around two-thirds of epileptic sufferers can be effectively managed and made seizure-free. Antiepileptic medications (AEDs) can help 60 percent to 70 percent of epileptic patients to live seizure-free with the right medication.⁵ Unmanaged epilepsies, on the other hand, does not automatically reflect treatment resistance.⁶ There can be a variety of reasons for the epilepsy’s uncontrollability. It’s possible that a person’s episodes aren’t epileptic. Uncontrolled epilepsy could also be the result of an individual being medicated with the incorrect AEDs, or with inadequate AED dosages, or it could be true drug-resistant epilepsy. At last, some individuals may have been appropriately identified, be on the right dose of the right AEDs, but still be uncontrollable due to noncompliance. According to a study, non-compliance ranged from 26% to 79 percent, with the wide variation among studies attributed to varied interpretations of compliance and cutoff values for identifying non-compliance.⁷ Epileptic individuals who do not follow their
AED treatment programs risk recurrence, status epilepticus, hospitalization, and higher health-care expenses. In epilepsy, noncompliance may even be linked to abrupt, inexplicable death due to status epilepsy. With an epilepsy rate of at least 9.99 per 1000 people in Pakistan, noncompliance and its consequences take on a significant dimension. There is a paucity of data on the incidence of AED non-compliance in the Pakistani epileptic patients, and much less is documented about the variables that contribute to it. Knowledge on the degree of non-compliance and the variables that may contribute to it could be useful in developing effective interventions. In this study, we determined the factors influencing antiepileptic drug (AED) nonadherence in a tertiary care hospital.

**Study design:** A cross-sectional study

**Place and Duration:** This study was conducted at Chandka Medical College Hospital at SMBBMU Larkana, Pakistan from January 2020 to January 2021.

**METHODOLOGY**

A predictive subgroup assessment to examine compliance was planned. In this study, all epileptic participants who presented to the Neurology outpatient department for the first session were recruited, but only those who were 18 years or above. We eliminated younger participants since compliance was measured using a self-reported scale, and its validity in younger participants was unknown. Treatment-naïve individuals, individuals using only conventional medicines, and individuals with cognitive decline severe enough to limit memory and/or contact with researchers were also excluded. The research was authorized by the institutional ethics review board after all participants signed a formal informed consent statement.

Epilepsy is a neurological illness that is characterized by frequent and unexpected disruptions of regular brain functioning, known as epileptic seizures. Adherence is defined as “The degree to which an individual’s behavior while consuming medicine coincides with agreed upon suggestions from a health care practitioner.” Nonadherence is described as any divergence from a recommended regimen’s instructions, both in terms of time and amount. An individual was identified with epilepsy if he or she experienced at minimum 2 uncontrolled seizures that occurred greater than 24 hours apart, or even a single uncontrolled seizure with a substantial risk of subsequent seizures. If the participant’s seizure semiology indicated that nonepileptic seizures were probable, it was defined as nonepileptic seizures. The revenue of the individual and his or her family was assessed and classified using modified Kuppuswamy and B G Prasad social economic levels to estimate income levels. M.I.N.I. (Mini International Neuropsychiatric Interview) was used to evaluate psychiatric comorbidities. The intensity of negative medication occurrences was graded using the Common Terminology Criteria for Adverse Events (CTCAE) scoring system. The monthly expense of all recommended medications, comprising of AEDs, vitamins, and calcium, was totaled to determine the medical costs. We left out the expense of diagnostic testing, travel fees, and any other costs associated with patient treatment. Polytherapy was described as the simultaneous use of two or several antiepileptic medicines. Seizures were classified as “often” if they happened more than once per month, and “uncommon” if they occurred less than once per month.

The four-item Morisky Medication Adherence Scale, a standardized, established survey for monitoring self-reported medication compliance, was used to evaluate compliance to AED therapy. The MMAS4 assesses whether the participant: (a) has ever neglected to consume medicine; (b) has ever experienced difficulty recalling to administer medication; (c) has ever discontinued medication due to improved symptoms; and (d) has ever discontinued medicine owing to deteriorating symptoms. Each item is given a score of 0 (Yes) or 1 (No). The ratings of each item are then added together to get a spectrum of scores ranging from 0 through 4. A rating of 3–4 indicates that the individual is compliant, whereas a rating of 2 indicates that the individual is noncompliant. In order to avoid recall biases, we concentrated on compliance in the four weeks leading up to the present outpatient clinic appointment.

An already structured proposal was used to gather data on demographics, epilepsy kind, psychiatric disorders, number of AEDs, length of treatment, drug-related negative occurrences, monthly expense of medication, and self-reported medication compliance.

Two objectives were of particular relevance to us: (a) estimating the percentage of epileptic individuals who were non-compliant to medicine according on MMAS4 and (b) variables related with AED non-compliance.

Microsoft Excel spreadsheets were used to input the data. To summarize initial variables, descriptive statistics were employed. Averages were used to display uninterrupted data with a normal distribution. Figures and percentages were used to depict categorical variables. The independent ‘t’ test was used to evaluate uninterrupted data, and the Chi-square test was used to evaluate categorical data. Univariate analysis logistic regression analysis was used to look at possible indicators of non-compliance. To develop the multivariable model, we utilized Hosmer and Lemeshow intentioned multivariable analysis with the goal of finding the most possible independent factors. All variables that indicated a possible effect in the bivariate analyses (i.e., variables with a P value just under 0.25 or medically meaningful) were incorporated in the multivariate analysis to develop the optimal model.
P-values less than 0.05 were considered significant in the final version. All of the statistical analyses were done with STATA version 13 program.

RESULTS

A total of 426 individuals were evaluated between the study duration. A total of 270 patients met the eligibility requirements and were enrolled in this subgroup study. Over the four weeks before the present outpatient clinic appointment, 82 (31%) of the individuals (n = 270) were noncompliant to medicine, whereas 188 (71%) were compliant. Table 1 shows the demographics of the individuals in the research. Using univariate regression assessment, there was a statistically substantial variation between compliant and noncompliant groups in epilepsy kind, AED polytherapy, monthly medicine expense, recurrent seizures, associated with drug side events, and length of treatment [As shown in Table 1]. Only three characteristics were identified to be linked with poor compliance in a multivariable iterative logistic regression assessment [As shown in Table 2]. AED polytherapy participants [OR: 4.4 (2.1-9.4) P = 0.002], with drug-related side effects [OR: 3.9 (2.2-7.4) P = 0.002] and a duration of therapy of more than 3 years for epilepsy [OR: P= 0.001] were the ones most likely to be linked to Noncompliance with AEDs [As shown in Table 2].

Table 1: Participants' demographic and clinical features

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Non-Compliant N=82</th>
<th>Compliant N=188</th>
<th>P-value</th>
<th>Univariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Mean (SD)</td>
<td>32.2 (+13.8)</td>
<td>31.5 (+12.4)</td>
<td>0.8</td>
<td>1.1 (0.9-1.1)</td>
</tr>
<tr>
<td>Male gender</td>
<td>44 (55.5)</td>
<td>111 (59.8)</td>
<td>0.4</td>
<td>0.7 (0.4-1.4)</td>
</tr>
<tr>
<td>Rural resident</td>
<td>36 (43.3)</td>
<td>78 (41.2)</td>
<td>0.5</td>
<td>1.0 (0.6-1.7)</td>
</tr>
<tr>
<td>Education less than matriculation</td>
<td>34 (43.4)</td>
<td>63 (34.1)</td>
<td>0.2</td>
<td>1.4 (0.8-2.3)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>24 (28.5)</td>
<td>60 (31.6)</td>
<td>0.5</td>
<td>0.6 (0.5-1.4)</td>
</tr>
<tr>
<td>Low socio-economic class</td>
<td>37 (46.8)</td>
<td>76 (41.1)</td>
<td>0.6</td>
<td>1.1 (0.7-2.2)</td>
</tr>
<tr>
<td>Marital status (single)</td>
<td>44 (52.2)</td>
<td>97 (51.4)</td>
<td>0.7</td>
<td>1.2 (0.7-1.8)</td>
</tr>
<tr>
<td>Epilepsy duration mean (SD)</td>
<td>5.4 (+7.3)</td>
<td>5.3 (+5.2)</td>
<td>0.8</td>
<td>1.1 (0.9-1.05)</td>
</tr>
<tr>
<td>Focal epilepsy</td>
<td>63 (76.6)</td>
<td>120 (63.7)</td>
<td>0.05</td>
<td>1.7 (1.02-3.2)</td>
</tr>
<tr>
<td>Generalized epilepsy</td>
<td>12 (16.55)</td>
<td>48 (26.1)</td>
<td>0.06</td>
<td>0.5 (0.4-1.05)</td>
</tr>
<tr>
<td>Uncertain epilepsy</td>
<td>7 (7.5)</td>
<td>20 (10.2)</td>
<td>0.4</td>
<td>0.7 (0.3-1.7)</td>
</tr>
<tr>
<td>Recurrent seizures</td>
<td>30 (38.1)</td>
<td>49 (26.6)</td>
<td>0.07</td>
<td>1.7 (0.8-2.9)</td>
</tr>
<tr>
<td>AED Polytherapy</td>
<td>70 (85.2)</td>
<td>81 (42.9)</td>
<td>0.002</td>
<td>7.7 (3.8-15.1)</td>
</tr>
<tr>
<td>Expense of Medication</td>
<td>1385.5</td>
<td>1038.1</td>
<td>0.001</td>
<td>1.1 (1.01-1.06)</td>
</tr>
<tr>
<td>Length of treatment (&gt;3 years)</td>
<td>56 (68.1)</td>
<td>54 (23.4)</td>
<td>0.002</td>
<td>5.2 (3.0-9.3)</td>
</tr>
<tr>
<td>Psychiatric comorbidity</td>
<td>15 (19.6)</td>
<td>26 (14.3)</td>
<td>0.26</td>
<td>1.2 (0.7-2.9)</td>
</tr>
</tbody>
</table>

Table 2: A multivariable logistic regression analysis was used to forecast factors linked to non-compliance to AEDs

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Non-compliance</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal epilepsy</td>
<td>1.4 (0.6-2.6)</td>
<td>0.41</td>
</tr>
<tr>
<td>AED Poly therapy</td>
<td>4.4 (2.1-9.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>Expense of medication</td>
<td>1.1 (0.9-1.1)</td>
<td>0.10</td>
</tr>
<tr>
<td>Negative effects associated with drug use</td>
<td>3.9 (2.2-7.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>Length of treatment (&gt;3 years)</td>
<td>2.5 (1.4-5.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Recurrent seizure</td>
<td>1.1 (0.7-2.3)</td>
<td>0.50</td>
</tr>
</tbody>
</table>
DISCUSSION

Medicine adherence can be understood as a treatment partnership between the physician and the patient, in which the clinician prescribes a medical prescription and the patient is required to follow it. The important problems of significance, when evaluating compliance are that the definition(s) of compliance are apparent, that a differentiation is established between the many forms of non-compliance, that the means of evaluating compliance are transparent, and that the consequence of non-compliance is clearly understood.

In the four weeks following the present outpatient clinic appointment, 31 percent of epilepsy patients were non-compliance to recommended AED medication. According to the research, lack of adherence ranged from 26 to 79 percent. This discrepancy could be due to differences in the study population’s demographics, definition of terms, and compliance assessment scales. AED polytherapy, drug-related unpleasant outcomes, and length of treatment greater than 3 years were the three characteristics we observed to be linked with non-adherence.

Whenever a society reports a big treatment gap, one automatically wonders of individuals who have never been identified or begun AEDs. Whilst such patients are a significant part of the treatment gap, there are multiple layers to the issue. The term “secondary treatment gap” refers to people who were identified and began AEDs at some time but then stopped taking them. Noncompliance on a regular basis may also result in a subsequent therapy gap. This issue is exacerbated in areas where epileptic patients are impoverished and unable to afford AEDs, are typically uninformed about epilepsy, are skeptical of contemporary treatment, and are afflicted by superstitions and culturally stigma. Epilepsy awareness promotes compliance. Participants that were part of this research were new to our hospital. At least 40% of these individuals did not require tertiary care. Despite this, we observed that a considerable number of participants were presently on polytherapy—85% in the non-compliant group and 43% in the compliant group. Extensive and frequently unjustified usage of polytherapy reveals a lack of consistency in the nation’s epilepsy prescription standards. Polypharmacy overuse gives little advantage in symptom control while increasing needlessly AED-related adverse consequences and raising medical costs. Although our study did not explicitly link medication costs to non-compliance, it is possible that non-compliance to polytherapy is partly due to the cost of healthcare. A higher cost is associated with a prolonged medication period. Individuals who have been on AED medication for a long time may have non-compliance as a result of not being educated about the necessity for continued treatment. Patients who are better educated about epilepsy, along with the anticipated length of therapy and the risk for AED-related side effects and how to minimize them, are more probable to stick to their treatment regimens.

Individuals self-reported AED non-compliance, and some cases of skipping the medication may have been ignored or even purposely hidden, which limits our study. We attempted to reduce recall bias by analyzing noncompliance in the four weeks leading up to the present appointment. Individuals may suppress data concerning noncompliance owing to humiliation or a worry of upsetting the treating physician on rare occasions.

Completing suitable boxes on the MMAS4 form in relative confidentiality and security constitutes self-reporting the MMAS4. We expect that this has allayed any anxieties or apprehensions patients may have had about disclosing non-compliance. Other diseases and coexisting non-AED pharmacies were not considered in our analysis, which contained mental disorders and AED pharmacy information.

Although a planned study with a bigger sample number may produce more accurate data, we believe our findings are significant for two justifications: (1) There is little reliable information about poor adherence in Pakistani epileptic patients, and (2) the variables that cause non-compliance are, for the most part, reparable.

CONCLUSION

Almost one third of the participants did not take their medicine as prescribed. Nonadherence may be minimized if patients’ treatments are limited to monotherapy as much as feasible and patients are provided ample knowledge, particularly about the length of treatment and the harmful consequences of AEDs.

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REFERENCES