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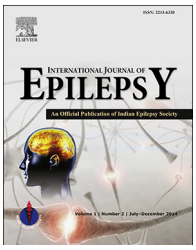

Original Article

Time to treatment predicts seizure outcome in a high-treatment gap epilepsy population

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ABSTRACT

Objectives: To investigate the relationship between time to antiepileptic drug (AED) treatment (TTT) and seizure outcome in a high treatment gap sub-Sahara African setting.
Methods: Clinical and demographic characteristics of 72 adults with epilepsy aged 18–75 years were obtained. We estimated TTT as the difference between the duration of epilepsy and the duration of treatment. Indices of clinical outcome including seizure severity and 6-month disease remission were documented. The effects of TTT and other clinical and demographic characteristics on clinical outcomes were tested using bivariate and logistic regression analyses.
Results: Forty (55.6%) of the participants initiated treatment within 5 years of seizure onset (TTT ≤ 5 years) while 32 (44.4%) initiated treatment after 5 years (TTT > 5 years). There was moderate to strong correlation between TTT and age of onset ($p = .009$), age at treatment initiation ($p = .026$), duration of epilepsy ($p = .000$), and seizure severity ($p = .020$). The TTT > 5 years group had an earlier mean age of onset ($p = .015$) and higher seizure severity score ($p = .001$) and were less likely to be in 6-month disease remission ($p = .014$). Time to treatment ≤5 years was the only independent predictor of lesser seizure severity (OR = 0.163, 95% CI = 0.041–0.649) and better 6-month remission (OR = 0.154, 95% CI = 0.031–0.770) after adjusting for age of onset, duration of epilepsy, and number of AEDs.
Conclusion: Delayed treatment initiation is common in our sample and independently associated with poor seizure outcome.

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1. Introduction

Epilepsy is associated with psychosocial consequences, such as social stigma and discrimination, which are often severe enough to force people with the disorder ''into the shadows''.[1] Consequently, a substantial number of people with epilepsy often remain undiagnosed and untreated.[1] This is partly responsible for the wide epilepsy treatment gap in some African countries estimated to be up to 95%.[2] Without treatment, the probability of long-term remission is 30–42%[3–5] while with treatment, it is 65–80%.[6–10] A large proportion of people with untreated epilepsy will therefore experience continued seizures and this may have enormous implications for outcome when treatment is instituted eventually.[4]

Studies of the prognosis of epilepsy have demonstrated a significant increase in risk for seizure recurrence with increasing numbers of seizures[11] and a decrease in the likelihood of remission following treatment in individuals with large numbers of seizures prior to treatment.[12–14] Continued occurrence of seizures also has the facility to cause changes to the ultrastucture of the brain which are not found in people with well controlled epilepsy.[15,16] It then follows that the time spent with untreated epilepsy may be as important as the absolute duration of the disease and the duration of its treatment in the prediction of long-term clinical outcomes in epilepsy.

However, while many studies have related the durations of epilepsy and its treatment and other time-related factors to the outcome of epilepsy, the time interval between epilepsy onset and treatment initiation has not been related to epilepsy outcome in many studies, particularly in wide treatment gap settings. In this study, we therefore, investigated the demographic and clinical factors associated with prolonged time ''in the shadows'' and its predictive effect on select clinical outcome indices of treated epilepsy.

2. Materials and methods

2.1. *Participants and procedures*

A total of 72 adult patients between the ages of 18 and 75 years with a diagnosis of epilepsy seen at the neurology clinic of the University College Hospital, Ibadan, Nigeria, were enrolled into the study. Criteria for inclusion in the study were a history of two or more unprovoked seizures and informed consent. Demographic data including age, sex, marital status, highest formal educational level, employment status, average monthly income, ethnicity, and religion were obtained. Disease-related variables including seizure frequency and type, etiology and class of epilepsy, duration of epilepsy, duration of treatment, and number of antiepileptic drugs (AEDs) were also obtained. Classification of epileptic seizures were based on the International League Against Epilepsy (ILAE) guidelines.[7,17] The indices of clinical outcome used were seizure severity, seizure freedom, and number of antiepileptic drugs. Time to treatment (TTT) (in years) was estimated from the difference between the duration of the disease and the duration of treatment. TTT was then dichotomized into ≤5 years (TTT ≤ 5 years) and >5 years (TTT > 5 years). All data were obtained from the patients and their case records.

The subjects were stratified into four seizure-specific severity groups (seizure free, low, moderate, and high seizure severity categories) based on the number of seizures in the previous 6 months and seizure type. This was a modification of the criteria for seizure-specific categorization of severity of epilepsy developed by Devinsky et al.[18] This scheme stratifies patients into seizure severity categories based on the number of seizures in the previous year and seizure type such that low, moderate, and high seizure severity levels for simple partial and absence seizures correspond to 1–20, 21–100, and 101–200 seizures, respectively, in the previous year. For complex partial seizures, low, moderate, and severe seizure severity correspond to 1–4, 5–12, and 13–24 seizures, respectively in the previous year, while for generalized tonic-clonic seizures, they correspond to 1, 2–4, and 5–12 seizures, respectively in the previous year. In this study, this was modified by obtaining seizure frequency data in the previous 6 months, therefore, half the seizure frequencies required were used for categorization into seizure severity groups. A score of zero was assigned to seizure freedom, while scores of 1, 2, and 3 were assigned to the low, moderate, and seizure severity levels, respectively.

2.2. *Statistical analysis*

The demographic and clinical characteristics of the subjects were summarized using the Student's *t*-test and univariate chi-square test. Analysis of the relationship between dichotomized TTT and continuous variables was done using Student's *t*-test. Relationship between dichotomized TTT and categorical variables was analyzed using univariate chi-square test. To determine the independence of TTT in the prediction of seizure severity and seizure freedom, a binary logistic regression model was constructed. For this purpose, seizure severity was dichotomized with scores of 0 and 1 in a group and 2 and 3 in another group. A 5% statistical significance level was chosen. The Statistical Package for the Social Sciences (SPSS), version 16 (SPSS Inc., Chicago, IL, U.S.A.) was used for all analyses.

2.3. *Ethical clearance*

Ethical clearance was obtained from the Health Research Ethics Committee of the University of Ibadan/University College Hospital, Ibadan, Nigeria.

3. Results

3.1. *Demographic and clinical characteristics of the study participants*

The mean age of the participants was 33.7 years (range 18–75 years) and 55.6% were male. About 87% were either students or in paid employment with slightly more than half earning up to 40 dollar equivalent a month (about 60% earned up to a dollar a day) (Table 1). Focal seizures were the most common seizure type (88.9%) with dyscognitive symptoms