Factors affecting adherence to antiepileptic medications among Sudanese individuals with epilepsy: A cross-sectional survey

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ABSTRACT

Background: Nonadherence to medication is widespread in epilepsy and other chronic diseases. Studies reporting adherence to antiepileptic medications are very limited in African countries. Adherence reports from low income African countries are few in contrast to multiple studies from high-income countries. Therefore, the aim of this study is to measure the level of adherence to antiepileptic medication in Sudanese population. **Methods:** A descriptive cross-sectional study of 96 individuals with epilepsy recruited from neurology outpatient clinics in three tertiary centers in Sudan. Data were collected by using a structured questionnaire containing Morisky Medication Adherence Scale-4 (MMAS-4) and Belief about Medication Questionnaire and analyzed by statistical package of social sciences. **Results:** About 35% of patients were estimated to be nonadherent. Most of the patients (93%) acknowledged their need for antiepileptic drugs. However, 35% had high concern score. Adherence is affected by attitude toward antiepileptic drugs (AEDs) and presence of side effects to AEDs. The relation between side effects and adherence was significant (*P* value 0.000). Furthermore, there was a statistically insignificant relation between the number of drugs used and adherence (*P* value 0.002). There was a significant relation between adherence, necessity mean score, concern mean score, and necessity concern differential *P* value 0.000 for all. **Conclusion:** Nonadherence to antiepileptic medication was reported in almost in one third of individuals in this cohort. There were statistically significant associations between nonadherence and both side effects and number of medications used in the treatment of epilepsy. Therefore, family physician should always check compliance with antiepileptic medication. Patient's education about adherence to medication through family physician may in part decrease the recurrence of epileptic seizures. Further research is needed to explore ways to increase adherence with AEDs in a low resource country like Sudan.

Keywords: Adherence, antiepileptic medications, epilepsy, Omdurman

Introduction

The management of epilepsy is complex as it involves avoidance of precipitating factors as well as suppression of recurrent seizure by prophylactic therapy with antiepileptic medication or surgery. Epilepsy has a relatively high prevalence, which is estimated to be 5 to 10 persons per 1000. In developed countries, the incidence rate ranges from 24 to 53 per 100,000 person-years.[1,2] Antiepileptic drugs (AEDs) can prevent seizures in approximately 70% of adult patients with epilepsy.[3] However, AEDs nonadherence is highly prevalent, with estimates ranging from 20% to 80%.[4] Nonadherence to AEDs is associated with increased risk of mortality, and a higher incidence of emergency

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department visits, hospital admissions, injuries, and fractures.[5] Generally, factors affecting adherence to medication can range from sociodemographic factors, such as age, gender, level of education, affordability, number of drugs administered, social support, beliefs about medication, and side effects to medication. It worth mentioning, it is preferable to maintain a patient on a single AED. This increases the probability of compliance, provides a wider therapeutic index, and is more cost-effective than combination drug treatment. Monotherapy in contrast to polytherapy is also associated with fewer idiosyncratic reactions and a lower incidence of teratogenic effects. Combination therapy can be associated with drug interactions between AEDs making it difficult to dose and monitor patients.[6]

Adherence (compliance) to a medication regimen is generally defined as the extent to which patients take medications as prescribed by their health care providers.[7] Adherence rates are typically higher among patients with acute conditions than chronic ones in which it drops dramatically after the first 6 months of therapy.[6-8] Adherence to antiepileptic medication predict better outcomes and collecting adherence data from subjects is now considered an essential part of several studies to ensure better compliance.[9-15]

Causes of nonadherence

Different methods are used in measurement of adherence. For example, self-reporting can be considered as a simple and effective measure, direct and indirect method can also come with advantage of increasing accuracy.[16,17] Importantly, no method is considered the gold standard.[5,18,19] Indictors of poor adherence will help physicians to identify patients who are most in need of interventions to improve adherence.[20-22] These indicators include depression, cognitive impairment, treatment of asymptomatic disease, inadequate follow-up or discharge planning, side effects of medication, lack of belief in treatment benefits, patients lack of insight into illness, poor provider-patient relationship, presence of barriers to care and medication, missed appointments, complexity of treatment, and cost of medication.[20-22] Importantly, reasons cited by patients (cited in order of high prevalence) for poor adherence were forgetfulness, other priorities, decision to omit doses, lack of information, and emotional factors, while 27% of the respondents did not provide a reason for poor adherence to a regimen.[5] Physicians contribute to patients' poor adherence by prescribing complex regimens leading to multiple issues in concern to adherence.[23-25]

McAuley *et al.* showed that patients with higher depressed mood scores were more likely to be nonadherent.[26] Chen *et al.*, showed that weight gain associated with AEDs (in particular pregabalin, phenytoin, and valproic acid) can also be one of the important cosmetic side effect to be no adherent.[27] Other studies reported cognitive side effect in addition to idiosyncratic effects, such as skin rashes, chronic effects, and weight gain, can lead to high rates of treatment discontinuation and complicate clinical management.[28-31] It worth mentioning poor adherence was also reported in secondary care and in the developed countries. For example, adherence in

secondary care showed that 59% of patients were nonadherent, while in USA 29% were nonadherent.[32,33] In China, Tang, *et al.* using Morisky Medication Adherence Scale-4 (MMAS-4). The results showed that of the 131 patients 4%, 70%, and 25% showed high, medium, and low adherence, respectively. The reasons for nonadherence included forgetfulness (54%), being seizure-free for a period (48%), and fear of adverse drug effects (27%).[29] In Nigeria, Sanya *et al.* showed that 21 (21%) did not comply with the use of given AED.[34] While in a primary care study in the UK showed that 36% of the patients were nonadherent. A total of 15% had low necessity scores, while 36% had strong concerns about AEDs, i.e. >midpoint scales. Nonadherent patients are expected to have low necessity in contrast to high concerns making the necessity concern differential (NCD) score low percentage.[35] The main objective of our study was to measure the level of adherence to AEDs among 96 Sudanese patients with epilepsy. Other minor objectives were to determine side effects of AEDs which are intolerable to patients and to assess the relation between patients' beliefs about their medication and adherence to medication. To our knowledge, this first study in Sudan to explore these issues of adherence to AEDs.

Methods

This was a descriptive cross-sectional multicenter hospital-based study between July 2015 and October 2015. The sample size was 96 represented all adult patients who were diagnosed with epilepsy for at least 6 months and enrolled from three major tertiary centers (Omdurman Teaching Hospital, Altigani Almahi Psychiatry Hospital, and the national center for neurology and neurosurgery in Khartoum).

All Sudanese adult patients who were diagnosed as having epilepsy for at least 6 months, attending these centers and willing to participate were included in the study. We excluded those who refused to participate or those with incomplete information. Data have been obtained by direct interviewing the participants using a simple direct standardized questionnaire. Adherence was measured by using the MMAS 4 [Table 1].[36] It has moderate to high reliability and criterion validity in some studies.[37]

It is a generic self-reported, medication taking behavior scale used for a wide variety of medical conditions. It consists of four items with a scoring scheme of "Yes" = 0 and "No" = 1. The items are summed to give a range of scores from 0 to 4. Patients will be considered nonadherent if they scored 1 or more. The four questions are: 1) Do you ever forget to take your medicine? 2) Are you careless at times about taking your medicine? 3) Sometimes if you feel worse when you take the medicine, do you stop taking it?, and 4) When you feel better do you sometimes stop taking your medicine?

Table 1 : Morisky Medication Adherence Scale-4 (MMAS-4)	
Adherence	**MMAS-4**
Adherent	0
Nonadherent	1-2-3-4

Attitude toward medications is going to be measured using Belief about Medicines Questionnaire (BMQ).[19-22,38]

The BMQ-specific is also a self-report questionnaire. It comprises two five-item factors assessing beliefs about the necessity of prescribed medication (specific-necessity) and concerns about prescribed medication based on beliefs about the danger of dependence and long-term toxicity and the disruptive effects of medication (specific-concerns). Respondents indicate their degree of agreement with each statement on a five-point Likert scale, ranging from 1 = strongly disagree to 5 = strongly agree. Scores obtained for individual items within both scales are summed. Thus, total scores for the Necessity and Concerns Scales range from 5 to 25. A high score is defined as a score more than midpoint of the scale which is 15 points. If a patient scores more than or equal to 15 in the necessity (or concern) scale he is considered to have a high necessity (or concern) score, higher scores indicate stronger beliefs. If patient scores less than 15, he or she has a low necessity score which is indicating the reverse. A NCD is calculated as the difference between the necessity and the concerns scales, with a possible range of −20 to +20. This differential can be thought of as the cost–benefit analysis for each participant, for whom costs (concerns) are weighed against their perceived benefits (necessity beliefs).[39]

Data have been coded and analyzed using the statistical package of social sciences version 22. The data were presented by using descriptive statistics (frequency tables) and statistical tests of associations (χ^2 test).

Ethical clearance has been obtained from the relevant authorities in Sudan Medical Specialization Board and Ministry of Health. The aim of the study was explained to the participants and written consents were obtained.

Results

In this study a total of 96 epileptic patients were recruited, all of them attending neurology outpatient clinics. Two thirds of the participants were females. One third of the participants were students, the distribution of the demographic characteristics is shown in the [Table 2].

Adherence distribution showed that (64.6%) of patients were adherent with a MMAS score of 0, while 35.4% of the participants were nonadherent with MMAS score more than or equal to 1. In this study, there was no association between gender and adherence (p value = 0.227) [Table 3].

The mean age was 29 (SD 12.8). The most young age group (16–26 years) represented 51% and it was the largest age group encountered. Then 25% were between 27 and 37 years. The χ^2 test of association and cross-tabulation between adherence and age in this study showed that the eldest age group (49 to 59) was significantly the least adherent with 60% nonadherence compared to the other groups (p value = 0.015). The association between the level of education and adherence revealed insignificant results (p value = 0.101).

The type of seizures was generalized in (29.2%) of patients and partial in (70.8%) of patients. The type of epilepsy was idiopathic in (61.5%) of patients, symptomatic in (26%) of patients, and cryptogenic in (12.5%) of patients. A total of 90% of the participants were taken one type of AEDs, and there was no significant association between the number of drugs and adherence. However, there was a significant relation between the number of drugs used and side effects P value 0.002.

In our study, 53.1% of patients reported cognitive side effects to medication. Sedation was the most commonly reported side effect in 64% of patients followed by dizziness in 47% of patients. Headache and diplopia both occurred

Table 2: Demographic characteristics of the studied participants (*n*=96)

Demographics	Percentage
Gender:	
Males	33
Females	67
Age group:	
16-26	51
27-37	25
38-48	9
49-59	15
Educational level:	
Illiterate	6.2
Primary	39.5
Secondary	35.4
University	18.7
Residence:	
Khartoum state	77.1
Another states	22.9
Employment:	
Student	34.4%
Employed	21.9
Unemployed	31.2
Housewife	12.5

Table 3: Comparison between the means of the necessity, concerns and NCD scores among the adherent and nonadherent groups by using an independent sample T test (*n*=96)

Adherence level	No. of patients	Necessity score mean	Concern score means	NCD score means
Adherent	62	20.85	11.98	8.85
Nonadherent	34	19.06	15.26	3.79
Total	96	20.2 (SD 1.91)	13.45 (SD 3.5)	7.06 (SD 4.35)
P=value		0.000	0.000	0.000

in 35% of patients. Memory problems occurred in 17% of patients.

Out of 33 students participated in the study, 18% was experienced reduced academic performance. Hair loss and weight gain occurred in 25% and 9% of patients on sodium valproate respectively. In 5% of patients, the adverse effects lead to cessation of medications. The association between side effects and adherence showed a highly significant relationship (*P* value = 0.000). Among those who were adherent, the percentage of participants experienced side effects was lower than those who did not. Forgetfulness was the most common cause for nonadherence in 97% of nonadherent patients. This was most commonly reported with Carbamazepine which was used by 68% of our patients. The necessity score in 93% of the studied participants scored above the midpoint of the i.e. (15 points). The mean score was 20.2 (SD 1.91) when the independent sample T test of significance was performed. We found that the average score of the necessity scale was higher among the adherent group when compared with the nonadherent one (*p* value 0.000).

The concern score ranged from 8 minimum to 20 maximum. The mean was 13.14 (SD 3.5). (35%) scored above the midpoint, i.e. had a high concern level. The average score of the concern level was lower among the adherent group than the nonadherent one (*p* value 0.000) [Table 3].

The NCD was ranging from a minimum of -3 to a maximum of 14. The mean was 7.06 (SD 4.35). The NCD score mean was significantly higher in adherent patients than in nonadherent patients' *P* value 0.000. In this sample, 24% of patients could not buy their medications throughout the treatment period and 49% of patients had medical insurance. It was found that 78% of patients from this group are of low-income patients sought help by asking for free drugs offered by some hospitals or financial help.

Discussion

In this study, quantifying the level of adherence showed that 64% were adherent and 35% were nonadherent. While nonadherence in UK is estimated to be 36% and 59% in two studies.[32,35] In Nigeria, the prevalence of nonadherence was found to be 21% and in Uganda it was 46%.[34,40] The percentage was higher in a study which looked into the mortality of epilepsy among patients in an endemic area with onchocerciasis in Uganda (64%).[41] These differences in the level of adherence might be attributed to social, environmental, and racial differences. Social acceptance of the disease and support by closely knit families of epileptic patients can enhance adherence in African patients.

The correlation between adherence and age in this study showed that the eldest age group (49–59 years) was significantly the least adherent with 60% nonadherence rate compared to the other age groups in the same study (*p* value 0.015). This might be caused by the presence of other comorbidities necessitating the use

of a large number of drugs causing gastric upset or secondary depression from epilepsy. However, Ferrari *et al.* showed that the younger age group in 385 patients in Brazil was significantly more nonadherent.[42] Interestingly, the same author found that female gender is significantly associated with better adherence. Gender and level of education did not have a significant association to nonadherence in this study (*P* value = 0.101).

The issue of monotherapy and polytherapy has been an issue of debate in many studies. In our study, there was no significant difference in adherence between those on monotherapy 68% and polytherapy 31% (*P* value = 0.308). As expected in patients with polytherapy, they significantly experienced more side effects, *P* value = 0.002. However, other studies like Canevini *et al.* and others concluded that adverse effects did not vary between the two groups.[43] Despite the fact that weight gain occurred in 9% (in comparison with 5% in study by Chen *et al.*[27]), weight gain in Sudan can be regarded as sign of health and wealth in Sudanese culture. Other undetermined factors may have played a role in that as only 18% of our patients were on valproate which is likely the cause of weight gain in epileptic patients.

Cognitive side effects in our study were experienced by 53% of the study sample but when the patients in the study group were asked (do these side effects stop you from taking the drug?), only 3% answered yes so it was intolerable in only 3% of the study population. In contrast to the Arif *et al.* study[28] in which cognitive side-effects resulted in discontinuation of treatment in 12% in a sample more than 1000 patients with 5 years follow-up. The lower percentage in our study is likely representing the differences in sample size and the lack of follow-up in the study. Nevertheless, the relationship between nonadherence and presence of side effects has demonstrated a significant correlation between both. This shows that patients who complain of side effects are less likely to be adherent even if they do not attribute their nonadherence to their disapproval of side-effects of the drugs. In the study done by Witt *et al.* it was found that psychiatric and cognitive side effects are least accepted.

Assessment of the attitude of patients toward their medication has been evaluated using the BMQ-specific. The necessity score median was 20. Moreover, 93% of the patients scored more than the midpoint of the scale, i.e. they appreciated the need for medications. This is higher than that of Chapman *et al.* study,[35] which was 84%. Therefore, most of the patients in this study believe in the need for their AEDs very strongly. Indeed; the mean score of necessity showed a very small difference between those who are adherent (20.9) and those who are nonadherent (19.1). This stronger belief on the need of our drugs might be due also to family support and social and cultural differences in the different study areas. In underdeveloped countries, there is a more tendency to comply with doctors' recommendations and this if appropriately invested will lead to more adherence.

The concern score showed that 34 (35%) had high concern score (that is they scored above the midpoint of the scale). This

percentage is slightly less than that of Chapman in which 36% had a high concern score. The correlation between concern score and adherence showed that the nonadherent patients have significantly higher concern scores which were similarly concluded by Chapman *et al.* Subsequently, about a third of the patients are worried about the potential adverse effects of their AEDs.

The NCD showed that 6 out of 96 patients had negative NCD score which means that their concerns outweighed the need for their drugs and representing an extreme state of concerns. In three patients it was 0 which is quite a way from the mean which was 7 for the same group. The rest of the patients had a positive score implying that most patients feel more in need of AEDs than being worried about potential side effects. The correlation between the NCD and adherence showed that patients with higher NCD scores have significantly more adherence. This was similarly concluded by Chapman *et al.*[35] The inability to afford drugs is a nonintentional cause that can affect adherence. In our study, about (24%) could not afford their medication consistently throughout the treatment period. This result is far lower than reported in the literature for under developed countries.[44] This can be attributed to the fact that majority of patients with chronic diseases in Sudan are supported by governmental medical insurance.

This study is not without limitations. One limitation of this study is related to the relatively small number of patients in comparison to the regional and international studies. Moreover, there was no follow-up in this study. Another limitation is related to the recruitment of patients in capital Khartoum only. Despite these limitations, we consider the findings of this study are novel and we believe that the outcome of the study will help clinicians and health policy makers in Sudan to care well for individuals with epilepsy and on pharmacological therapy.

Conclusion

Nonadherence to antiepileptic medication was reported in almost in one third of individuals in this cohort. There were statistically significant associations between nonadherence and both side effects and number of medications used in the treatment of epilepsy. Therefore, family physician should always check compliance with antiepileptic medication. Patient education about adherence to medication through family physician may in part decrease the recurrence of epileptic seizures. Further research is needed to explore ways to increase adherence with AEDs.

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Conflicts of interest
There are no conflicts of interest.

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