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Prevalence and factors associated with non-adherence to antiepileptic drugs among children with epilepsy in Jos, Nigeria

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Abstract*:* *Background:* Childhood epilepsy causes a tremendous burden for the child, the family, society as well as the healthcare system. Adherence to antiepileptic drugs (AEDs) is key to treatment success, one of the main causes of unsuccessful treatment for epilepsy is poor adherence to medications. Non-adherence in children with epilepsy presents a potential ongoing challenge for achieving a key therapeutic goal of seizure control.

Aim: To determine the prevalence and factors associated with non-adherence to AEDs among children with epilepsy at Jos University Teaching Hospital, Jos, Nigeria.

Methodology: This cross sectional study was done to assess the prevalence and factors associated with non-adherence to AEDs among children with epilepsy from November 2019 to February 2020. A structured questionnaire was used to collect relevant information on the adherence of study subjects to AEDs based on self/caregiver report. Part of the questionnaire was derived from Morisky Medication Adherence Scale (MMAS-8).

Results: One hundred and ninety-four subjects were recruited for the study. The prevalence of non-adherence to AEDs was 44.8%. Factors significantly associated with non-adherence were low socioeconomic status, multiple drug therapy and long duration of treatment. The main reasons for non-adherence were financial constraint, forgetfulness, lack of improvement and medication side effects.

Conclusion: Non-adherence to medication is common among children with epilepsy and it hampers the key therapeutic goal of seizure control. Improving per capita income of families, providing universal health insurance, medication reminders and appropriate education/counseling will reduce non-adherence and improve the long term outcome of childhood epilepsy in our region.

Key words: Epilepsy, Children, Anti-epileptic drugs, Non-adherence, Prevalence, Associated factors, Jos, Nigeria.

Introduction

Epilepsy is a common chronic brain disorder characterized by recurrent seizures that affects people of all ages, all over the world.[1,2] The goal of treatment of epilepsy includes minimizing the risk of recurrent seizures and antiepileptic drug (AED) side effects, and maintaining normal psychosocial and educational/vocational adjustment.[3] Adherence to AEDs is key to treatment success, one of the main causes of unsuccessful drug treatment for epilepsy is poor adherence to prescribed medication.[4,5] Non-adherence in children with epilepsy presents a potential ongoing challenge for achieving a key therapeutic goal of seizure control.[6] Non-adherence to AEDs leads to inadequate treatment with subsequent uncontrolled seizures which leads to more emergency room visits, hospitalizations, poor quality of life, morbidity, and mortality.[7-12] This reduces the benefits that could be gained from the medication.

Non-adherence to medication is a complex problem that is influenced by many factors. According to the World Health Organization,[13] the factors affecting adherence can be grouped into the following five dimensions: socioeconomic-related factors, health care team/health system-related factors, condition-related factors, treatment-related factors, and patient-related factors. Patients may be non-adherent at any time during their treatment,[14] they may use more or less than the prescribed treatment or discontinue treatment prematurely.[15] The

prevalence of non-adherence to AEDs in patients with epilepsy generally tend to be high, ranging from 20% to 80% depending on the populations studied, definition used for non-adherence, and research methods.[16-19] The assessment of adherence should be a routine action in the management of epilepsy. Despite the lack of a gold standard for measuring adherence to medication, both direct and indirect measures are currently used in clinical practice.[20]

There is no published data on the prevalence and factors associated with non-adherence to AEDs in children in Jos, Nigeria. The aim of this study was to determine the prevalence and factors associated with non-adherence to AEDs at Jos University Teaching Hospital, Jos, Plateau State, Nigeria.

Methodology
Study Site

This study was carried out at the pediatric neurology clinic of Jos University Teaching Hospital. The clinic runs every week at the pediatric out-patient department (POPD) of the hospital. It attends to about 40 patients every clinic day. About 50% of children attending the clinic have epilepsy.

The diagnosis of epilepsy was made by the Paediatrician after proper evaluation following two or more unprovoked seizures that occurred at least 24 hours apart. An electroencephalogram was used to support the diagnosis and properly classify the epileptic seizures in most cases. After diagnosis and counselling, an appropriate first-line AED was chosen, taking into account the seizure type, availability, cost and known side-effects. Patients were then followed up at the pediatric neurology clinic initially 2 weekly, then 4 weekly. Longer appointments were subsequently given when seizures are controlled. At every follow-up visit, clinical information and response to AED treatment were documented. Drug doses were gradually increased based on response and weight, and treatment was altered as clinically indicated. Monotherapy was used initially in all patients, additional AEDs were added if seizures were not fully controlled. Adherence to treatment regimen was monitored at the clinic.

Study Population

Subjects of the study were children less than 18 years of age with epilepsy who were on AEDs. Children on other medications because of other chronic illnesses were excluded from the study.

Study Design

This was a cross sectional study.

Sample size

The minimum sample size was calculated using the formula:[21]

$$\text{Sample size} = \frac{Z^2 P(1-P)}{d^2}$$

Where
Z = standard normal variate set at 1.96 for 2-tailed study
P = proportion of patients with non-adherence to AED from a study in South Africa.[22]
d = absolute error or precision set at 0.05
Sample size = 194

Data Collection

We used structured researcher-administered questionnaire to collect information from the caregivers of the subjects from November 2019 to February 2020. Some of the subjects who take medications by themselves also provided relevant information.

The questionnaire consisted of three sections. Section 1 contained information on socio-demographic data. Section 2 which was derived from Morisky Medication Adherence Scale (MMAS-8)[23] was used to assess adherence based on self/caregiver report. The scale is composed of 8 items. Items 1-7, except item 5, are yes/no questions, where no answers receive a score of 1 while yes answers receive a score of 0. For item 5, the score is reversed. Item 8 is measured based on 1-5 Likert scale. The total scores range between 0 and 8, where 8 is regarded as high adherence, 6-7 moderate adherence, and less than 6 low adherence. Based on the scale, patients who scored less than 6 were classified as non-adherent. The MMAS-8 has widespread acceptance in clinical settings and has been found to be internally consistent and validated in Nigeria.[24] Advantages of MMAS-8 include cost-effectiveness, ease of use and convenience. Disadvantages of the scale include recall bias and participants feeling pressured to give acceptable responses in an effort to elicit positive reaction from their healthcare provider. Section 3 contained information on reasons for on-adherence.

Data Analysis

Data obtained was analyzed with statistical package for social sciences (SPSS) software version 20. Results were presented in descriptive statistics using frequency tables. Chi-square test was used to determine significance of association between non - adherence and patients' characteristics. *P* value <0.05 was considered significant.

Ethical Consideration

Ethical approval for the study was obtained from the Health Research and Ethics Committee of Jos University Teaching Hospital. Written informed consent was obtained from the caregivers of the subjects and verbal assent was obtained from subjects that were 6 years of age.

Results

A total of 194 subjects were recruited for the study. The mean age of the subjects was 7.14±2.82 years (age range 4 months to 16 years). The characteristics of the subjects are shown in table 1.

Out of the 194 patients, 87 (44.8%) had low adherence (non-adherence) to AEDs, 34 (17.5%) had moderate adherence while 73 (37.6%) had high adherence. Table 2 shows factors associated with non-adherence to AED.

Factors that were significantly associated with non-adherence were low socioeconomic class, polytherapy and AED therapy for >12 months (*P*=0.002, 0.003 and 0.02 respectively).

The commonest reason for non-adherence was financial constraint followed by forgetfulness, lack of improvement and side effects of medications. Some have multiple reasons for being non-adherent (Table 3). A disproportionate number of patients that take medications by themselves report forgetfulness as the major reason for non-adherence.

Table 1: Characteristics of the patients

Characteristics	n (%)
Sex	
Male	101 (52.1)
Female	93 (47.9)
Age	
<1 year	7 (3.6)
1-5 years	72 (37.1)
6-10 years	93 (47.9)
11-17 years	22 (11.3)
Primary caregiver	
Mother	147 (75.7)
Father	14 (7.2)
Sibling	5 (2.6)
Grandparents	19 (9.8)
Uncle/Aunt	5 (2.6)
Others	4 (2.1)
Caregiver educational status	
None	29 (15.0)
Primary	53 (27.3)
Secondary	78 (40.2)
Tertiary	34 (17.5)
Socio-economic status	
Upper class	52 (26.8)
Middle class	34 (17.5)
Lower class	108 (55.7)
Type of epilepsy	
Generalized	148 (76.3)
Focal	46 (23.7)
Number of AEDs	
One	115 (59.3)
Two	62 (31.9)
Three	13 (6.7)
Four	4 (2.1)
Duration of AED therapy	
<6 months	24 (12.4)
6-12 months	41 (21.1)
13-24 months	102 (52.6)
>24 months	27 (13.9)

AED antiepileptic drug

Table 2: Factors associated with non-adherence to AED

Characteristics	Non-adherence	Adherence	Total (%)	x^2	*P* value
Sex				0.41	0.52
Male	48	53	101 (52.1)		
Female	39	54	93 (47.9)		
Age				0.93	0.34
<1 year	3	4	7 (3.6)		
1-5 years	38	34	72 (37.1)		
6-10 years	36	57	93 (47.9)		
11-17 years	10	12	22 (11.3)		
Caregiver educational status					
None	15	14	29 (15.0)	1.61	0.20
Primary	25	28	53 (27.3)		
Secondary	33	45	78 (40.2)		
Tertiary	14	20	34 (17.5)		
Socio-economic status					
Upper class	14	38	52 (26.9)	9.12	0.002
Middle class	15	19	34 (17.5)		
Lower class	58	50	108 (55.6)		
Type of epilepsy					
Generalized	72	76	148 (76.3)	3.03	0.08
Focal	15	31	46 (23.7)		
Number of AEDs					
Monotherapy	41	74	115 (59.3)	8.76	0.003
Polytherapy	46	33	79 (40.7)		
Duration of AED therapy					
<6 months	7	17	24 (12.4)	5.47	0.02
6-12 months	14	27	41 (21.1)		
13-24 months	49	53	102 (52.6)		
>24 months	17	10	27 (13.9)		

Table 3: Reasons for non-adherence to AEDs

Reason for non-adherence	n (%)
No money to buy drugs	43 (49.4)
Forgot to take drugs	32 (36.8)
No improvement	15 (17.2)
Side effects of medications	12 (13.8)
Medicine not available	8 (9.2)
Myths and beliefs about epilepsy	7 (8.1)
Seizures stopped	6 (6.9)
Frequency of drug administration	5 (5.7)
Lack of appropriate counseling	5 (5.7)
Child refused to take medications	4 (4.6)
School schedules	3 (3.5)
Inability to get prescription	2 (2.3)
Caregiver comes back late	2 (2.3)
Caregiver travelled	1 (1.2)
Child refuses to take drugs	1 (1.2)
Child went on holiday	1 (1.2)

Discussion

This study was carried out to ascertain the prevalence and factors associated with non-adherence to AEDs among children with epilepsy. The prevalence rate of non-adherence to AEDs in this study was 44.8%. The prevalence of non-adherence obtained in this study was high, this will jeopardize the goal of achieving seizure control in children with epilepsy in our community. Despite the fact that there are other causes of unsuccessful treatment of epilepsy such as epilepsy syndromes, substandard drugs and co-morbidities, adherence is key to treatment success. Non-adherence to AEDs invariably leads to uncontrolled seizures. Uncontrolled seizures

may result in emergency room visits and hospitalizations that will put further strain on the healthcare system and also deplete family resources. It can also cause brain damage that may lead to co-morbidities such as intellectual disability and behavioral abnormalities which will further worsen the long term outcome. Non-adherence could also lead to status epilepticus, a pediatric emergency with high incidence of mortality and severe brain damage.

The actual prevalence of non-adherence in this study may be higher because we used caregiver/self-report which has been shown to under-report non-adherence.[25] Self/caregiver report may be subject to recall bias as information provided may not be accurate and some may feel pressured to give acceptable responses in an effort to elicit positive reaction from the healthcare provider.

This prevalence rate is similar to the 45% reported by Jacobs et al in South Africa in 2016,[22] higher than the 20.5% reported by Nazziwa et al in Uganda in 2014[25] and Quol et al in Jordan in 2015[26] respectively, but lower than the 58% reported by Modi et al in USA in 2011.[6] The prevalence of non-adherence to AEDs in patients with epilepsy depends on several factors such as the populations studied, definition used for non-adherence, and research methods.[16-19] Similar to this study, the one done in Jordan used self/caregiver report. The study in South Africa used modified medicine possession ratio while the study in USA used electronic monitors to assess adherence. The study in Uganda which used both self-report and drug level monitoring found a wide disparity of non-adherence between the two methods (20.5% and 77.9% respectively).

Factors that were significantly associated with non-adherence to AEDs in this study were low socioeconomic status, multiple drug intake and long duration of therapy. Modi[27] also reported that family socioeconomic status was the only predictor of non-adherence to AEDs in children with epilepsy in United States of America in 2011. Income and social status are major determinants of health status of the people.[28] Because of scarce resources, families usually choose between providing food, shelter, and other necessary services including healthcare. This is worsened by lack of universal health insurance and relatively high cost of medications. Improving per capita income of families, providing universal health insurance, making first-line AEDs available and affordable will help improve adherence to AEDs in resource-limited countries.

Being on multiple drugs can lead to non-adherence in many ways. These include increased medication cost, pill burden and more adverse drug reactions (ADRs). Pill burden is particularly a problem in children and adolescents and refusal to take drugs is worse with increasing number of medications. Monotherapy for epilepsy is the standard management, polytherapy is more likely to be associated with drug toxicity.

Duration of therapy was also significantly associated with non-adherence. Those that had been on AED for >12 months had higher rate of non-adherence. This could result from medication fatigue on the part of the subjects or their caregivers, being seizure free or seizure still persisting while taking medications. Non-adherence is particularly a problem with chronic illnesses that require long duration of treatment and is a major problem facing medical practice.[29]

The commonest reason for non-adherence in this study was financial constraint in buying medications. In communities where drugs are not provided freely or at subsidized rate, non-adherence to medications is a major problem because families will prioritize other needs like food and shelter over drugs. This is particularly a problem in resource-limited countries.[30] This is similar to studies in Uganda[25] and Saudi Arabia[31] but contrasts with studies from other regions that reported forgetfulness as the major reason for non-adherence.[32-34]

Forgetfulness was the second commonest reason for non-adherence in our study. Caregiver may forget to give medications when he/she has busy schedules or when the child stops having seizures. Forgetfulness was also a major problem among children and adolescents who take their drugs by themselves without supervision. There is need to educate parents/caregivers to administer/supervise the administration of medication to children even when they think they are old enough to take medications by themselves. Counseling and ongoing counseling on the need for regular administration of AEDs even when seizures are controlled are of paramount importance.

Some of our patients stopped taking their medications because seizures were not controlled while taking AEDs with many of them resorting to alternative therapy only to return when those alternatives fail. Epilepsy is sometimes associated with spiritual attack in our community and some people believe it should not be treated with orthodox medicine. This is usually reinforced when seizures are not controlled after taking AEDs for some time. More public awareness on the etiology and treatment of epilepsy needs to be done in order to reduce the myths and stigma associated with the disorder and improve adherence to AEDs.

The 4th commonest reason for non-adherence in our study was side effects of medications. Adequate counseling on the possible side effects of the prescribed medication at commencement of AEDs could help prepare patients to better manage medication side effects and reduce non-adherence. Most side effects of AEDs are mild and usually subside within weeks and may not require discontinuing the drug.

This study has some limitations. Firstly adherence was assessed by self/caregiver report which may not be very reliable. Nazziwa et al reported a wide disparity between adherence self-report and serum drug level in Uganda.[25] Secondly the sample size was relatively small and we recommend a larger multi-centre study.

Conclusion

Adherence to AEDs is crucial in achieving the key

therapeutic goal of seizure control among children with epilepsy. The non-adherence rate of 44.8% reported in this study will hamper this goal. Factors associated with non-adherence include poor socio-economic status, polytherapy and long duration of therapy. Main reasons for not adhering to medications were financial constraints, forgetfulness, lack of improvement and medication side effects. Improving per capita income of families, providing universal health insurance, medication reminders and appropriate education/counseling will reduce non-adherence and improve the long term outcome of childhood epilepsy in our region.

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