FACTORS AFFECTING COMPLIANCE TO TREATMENT AMONG CHILDREN WITH EPILEPSY ATTENDING AT A PAEDIATRIC NEUROLOGY CLINIC OF A TERTIARY HOSPITAL IN ENUGU

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ABSTRACT

BACKGROUND: This study aimed to determine the factors affecting compliance to treatment among children with epilepsy in Enugu, Nigeria.

METHODS: Children with diagnosis of epilepsy were consecutively recruited. Their 6 months retrospective and 1 month prospective data were collected; and analyzed using SPSS version 20.0 ($p < 0.05$).

RESULTS: Fifty six children with epilepsy (mean age= 9.7 ± 4.1 years) were studied. Generalized tonic clonic epilepsy was noted in 41.1% (23/56) of them. Thirty six (64.3%) complied strictly with the treatment regimen. Polytherapy, high cost of drugs, multiple drug dosages and drug related side effects affected compliance. Majority (79.4%, 27/34) of patients on monotherapy and a few (27.2%, 6/22) on poly-therapy had good seizure control ($p<0.001$).

CONCLUSION: Poor drug compliance is a major constraint to adequate seizure control in children with epilepsy in our setting. Addressing the problem of poor compliance will enable them to achieve optimal seizure control.

KEY WORDS: Epilepsy, Treatment Compliance, Associated Factors; Children

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INTRODUCTION

Epilepsy is an important public health problem particularly in developing countries with limited resource. Globally, its prevalence varies between 4.0 and 10 per 1000 population,[1,2] and has been reported to account for 60% of chronic neurological conditions seen in a tertiary paediatric neurology clinic in Enugu, South East Nigeria,[3] as well as one of every three children presenting at a paediatric neurology service in Ibadan, South West Nigeria.[4]

Poor compliance to treatment is a major factor affecting seizure control as well as quality of life of children with epilepsy. Approximately 30% - 70% of patients with chronic illnesses like epilepsy, asthma and diabetes have poor compliance/adherence to treatment as a result of the psychological, educational and social problems which surround these chronic illnesses.[5,6]

Several factors have been linked to poor compliance including extended treatment duration, periods of symptomatic remission, high cost of treatment, a shift in physician-patient relationship as well as medication related issues such as multiple medications, acceptability and palatability of the drug form, and adverse effects of the medication.[6,7] In resource limited settings like ours, high rates of low socio economic status including low literacy levels and poverty; social customs and cultural beliefs; high rates of social stigmatization further compound the problem of compliance among children with epilepsy.[8, 9, 10] The cultural beliefs that epilepsy is caused by supernatural powers, evil spirits, extremes of heat and cold, inhalation of bad air, contact with bad saliva and urine adversely affect compliance of children with epilepsy to treatment as caregivers seek traditional complementary and alternative medical care (CAM) either prior to initial presentation to hospital or in

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between periods of treatment.[7,8,11] The resultant effect is that patients present late to the clinics with some manifesting evidence of mental retardation and incapacitation requiring complete dependence on a caregiver to maintain the minimal level of quality of life.[12]

Generally, poor compliance could lead to poor seizure control[11] due to inadequate or unsuccessful therapy further reducing the quality of life of the sufferer. It creates room for unnecessarily extended treatment, additional clinic follow up visits, and change of medication regimen in order to improve their clinical condition.[13] Good treatment compliance in children with epilepsy will ensure adequate seizure control, improved academic performance as well as overall quality of life.[14]

Hence, the study was aimed at determining the factors affecting compliance to treatment among children with epilepsy attending the Paediatric Neurology Clinic University of Nigeria Teaching Hospital (UNTH), Ituku-Ozalla, Enugu, South East Nigeria

Methods

Study setting:

The paediatric neurology clinic is a weekly (Friday) clinic with full complement of staff. There are 3 trained paediatric neurologist, 2 senior registrars, and 3 registrars running each clinic day. Other support staff are the medical records officers who sort out patients' folders. Services rendered are mainly clinical. Electroencephalography is performed by trained EEG technicians on requests by attending neurologist. Other ancillary services provided are physiotherapy, speech therapy. Ophthalmology, Otorhinolaryngology and psychiatry consults are sought based on individual patient need etc. Children who require specialized education are referred to centers that offer such services.

Study Population:

Paediatric patients from 6 months to eighteen years old with neurological disorders such as post infectious neurological deficits, developmental delays, epilepsy or epileptic syndrome; behavioral disorders, pervasive disorders, children with single or isolated seizure, and recurrent febrile seizures make up the study population.

Study design:

This was a combined retrospective and prospective cohort study conducted over a 9 month period (1stJuly 2012 to 31st March 2013) in which patients with epilepsy who met the inclusion criteria were consecutively enrolled.

Case definitions:

A seizure is defined as a paroxysmal time-limited change in motor activity and/or behavior that results from abnormal electrical activity in the brain.[15]

Epilepsy is defined as two or more unprovoked seizures occurring at an interval greater than 24 hours apart or one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years or an epileptic syndrome.[16,17]

An epileptic or epilepsy syndrome is a cluster of seizures, other symptoms, physical signs and laboratory findings, which are associated in a non-fortuitous manner. Identification of an epileptic syndrome requires clinical findings (type of seizure, age at onset, precipitating factors, severity and chronicity, circadian distribution, aetiology, anatomical location and prognosis) and data from ancillary studies (electro-encephalogram (EEG), brain anatomical and metabolic imaging, haematology and biochemistry).[14]

The seizure types were classified based on the ILAE classification of epilepsy and epileptic syndromes.[18,19]

Inclusion Criteria:

All paediatric patients who were aged 1 to 18 years old diagnosed with epilepsy/ epilepsy syndrome from history, clinical examination, and Electroencephalogram (EEG) with or without computerized tomography scan (CT scan) and biochemical tests who had attended Paediatric Neurology Clinic of the University of Nigeria Teaching Hospital, Enugu for at least 6 months were the subjects of this study.

Exclusion Criteria:

Newly diagnosed patients with epilepsy as well as confirmed cases of other neurological disorders other than epilepsy or epileptic syndrome; children with single or isolated seizure, febrile or other provoked seizures; and patients who have been on remission not requiring antiepileptic drug were excluded.

Ethical Considerations:

Ethical approval for the study was obtained from the Health Research and Ethics Committee of the UNTH, Enugu. The objectives and details of the study were explained to patient's mothers/ caregivers, and older patients in a language that is well understood by them. Informed verbal consents were obtained from the patient's mothers/ caregivers, and assent was obtained from the children who were old enough to give

information about their conditions.

Data Collection

Relevant data was collected on each of the recruited patients using a standardized structured interviewer administered questionnaire[20] by one of the investigators. Data collected include: socio-demographic characteristics including name, age, gender, religious inclination, highest educational attainments as well as the occupation of the parents from where the socioeconomic class was determined using the method proposed by Oyedeji.[21] Other information obtained included clinical diagnosis, co-morbid medical conditions; spiritual illusion or thoughts of parent/caregiver about epilepsy; electroencephalographic and/ or CT scan report; seizure frequency; previous history of seizures including frequency and treatment received, treatment given in the neurology clinic, drug dosages, doses missed, compliance to drug regime/administration, adverse effects attributable to the drugs, any change in drug regimen, accessibility of drugs, duration of follow up/ period of default (default was defined as being more than 1 month late for the next scheduled appointment);[22] history of seizure recurrence and seizure frequency during discontinuation of treatment. Patients were followed up after enrollment for a period of 1 month during which additional information on seizure frequency during follow up was obtained. Drugs were supplied in a container and patients/ parents were advised to adhere strictly to prescription given. They were instructed to return the container and the remaining drugs during the next visit.

Measurement of Compliance and Seizure control:

Compliance was measured by the patient/ parent reported adherence to prescription in a questionnaire as well by pill counting. Patients were considered good compliers if they admitted to have taken their drugs as prescribed within the 7 months under review (last 6 months before the study and 1 month during the study), had not missed out-patient clinic visits more than once, and compliance was confirmed if they took > 85% of the medications prescribed for one month.[20]

Patients were considered controlled if they had two or fewer seizures during 7 months of known seizure treatment (i.e. last 6 months before the study; and 1 month during study)[20] and uncontrolled if they had 3 or more attacks during this period.

Data Analysis

The data obtained was analyzed with the computerized IBM Statistical Package for Social Sciences (SPSS) version 20 (IBM Chicago Illinois, USA). Characteristics were presented as frequency tables. Chi–square was used to test for statistically significant associations between variables. The level of statistical significance was set at $p < 0.05$.

Results

A total of 56 patients (36 males and 20 females) aged between 2 years to 18 years old (mean age: 9.7 ± 4.1 years) were studied. Twelve (21.4%) of the 56 patients were of the upper social class (I and II), 18 (32.1%) middle class (III), while 26 (46.4%) belonged to the lower class (IV and V), as shown in Table 1.

Table 1: Socio-demographic characteristics of 56 participants

	Frequency (n)	Percentage (%)
Age		
1-5	10	17.9
6-10	19	33.9
11-15	22	39.3
> 15	5	8.9
Gender		
Male	36	64.3
Female	20	35.7
Socioeconomic Class		
High	12	21.4
Middle	18	32.1
Low	26	46.4

The most frequent type of epilepsy was the generalized tonic clonic epilepsy occurring in 23/56 (41.1%) of patients followed by the mixed epilepsy seen in 9 (16%) of cases, and then complex partial seizure occurring in 7 (12.5%) of cases. The mixed epilepsy was a combination of generalized tonic clonic seizure with any of the following: complex partial, focal with secondary generalization, absence, atonic, or myoclonic seizures. One patient had infantile spasm, as displayed in Table 2.

Table 2: Types of Epilepsy based on Clinical Diagnosis among 56 participants

Type of Epilepsy	Frequency (n)	Percentage (%)
Generalized Tonic Clonic	23	41.1
Generalized Clonic	1	1.8
Generalized Tonic	3	5.4
Absence seizure	1	1.8
Simple Partial	2	3.6
Complex Partial Seizure	7	12.5
Partial Seizure with Secondary Generalization	3	5.4
Atonic	4	7.1
Myoclonic	2	3.6
Infantile spasm	1	1.8
Mixed Epilepsy	9	16.1
Total	**56**	**100**

Forty (71.4%) respondents did not know the possible causes of epilepsy; 13 (23.2%) responded to other causes such as hereditary, fever, brain trauma, brain tumor, malaria, breech delivery, transfusion of unscreened blood; 4 (7.1%) respondents feel epilepsy is caused by a combination of factors including anger of the ancestral spirits, evil spirit, extremes of heat and cold, and witches / wizards.

Twenty six (46.4%) sought treatment at various private clinics before presentation; 10 (17.9%) did not seek any form of treatment; 8 (14.3%) sought and received herbal medication; 7 (12.5%) resorted to prayers; 2 (3.7%) visited traditional healing homes. Only one respondent offered sacrifices to the gods.

The antiepileptic drugs used in treating these patients include- phenobarbital, carbamazepine, sodium valproate, phenytoin, nitrazepam and clonazepam. Carbamazepine was the most frequently used drug. The drugs were very accessible to about 89.3% of patients. Only 6 out of 56 patients experienced difficulty accessing their drugs. Three of them were on Tegretol-control release while the other 3 were on sodium valproate (Epilim).

A total of 36 (64.3%) respondents complied strictly with the treatment regimen while 20 (35.7%) were not compliant ($p<0.001$). Of these 20 who were not compliant, 14 had reasons for not being compliant (Table 3). The remaining 6 had no reasons. Thirty four (60.7%) patients were on single therapy; 22 (39.3%) were on multiple regimen (ranging between 2 to 4 drugs).

Table 3: Factors responsible for non-compliance among the 20 participants who did not comply with treatment

Reasons	No. of patients (n)	Percentage (%)
High cost of drugs	4	20
Forgot to take drugs	7	35
Felt the dose was too much	2	10
Had side effects	1	5
None	6	30
Total	**20**	**100**

Twenty four of 34 patients (70.6%) on single therapy and 12 of 22 patients (54.5%) on multiple drugs were compliant; 10 patients on single therapy and 10 patients on poly-therapy were not compliant as shown in Table 4 ($c^2= 1.497$; $p>0.05$).

Table 4: Relationship between Mode of therapy and Compliance among 56 participants

	Compliant n (%)	Not compliant n (%)	Total N (%)
Therapy			
Single	24 (70.6)	10 (29.4)	34(100)
Multiple	12 (54.5)	10 (45.5)	22 (100)
Total	36 (64.3)	20 (35.7)	56 (100)

$c^2=1.497$; $P= 0.262$

About 76.2% of patients on twice daily dosing were compliant; Only 28.6% of patients on three times daily dosing were compliant ($c^2= 10.370$; $p<0.05$), Table 5.

Table 5: Relationship between Drug Dosing and Compliance among 56 participants

	Compliant n (%)	Not compliant n (%)	Total N (%)
Drug Dosing			
Twice daily	32 (76.2)	10 (23.8)	42 (100)
Thrice daily	4 (28.6)	10 (71.4)	14 (100)
Total	36 (64.3)	20 (35.7)	56 (100)

$c^2=10.370$; $P= 0.001$ (significant)

Seizure control among patients on single therapy was compared with that of patients on poly- therapy. Twenty seven (79.4%) of 34 patients on single therapy had good seizure control while only 6 (27.2%) out of 22 of patients on poly-therapy were controlled (c^2= 15.003; p<0.001).

Thirty seven patients (66%) were not experiencing any form of side effects; 19 (34%) were experiencing side effects. Of the 19 who had side effects, 17 listed the specific side effects. Most common side effect noted was excessive sleep (5/56, 8.9%). Others were dizziness (2/56, 3.6%), hyperactivity (2/56, 3.6%), skin rash (2/56, 3.6%), weight gain (2/56, 3.6%). The least side effects were forgetfulness, generalized weakness, jerky movements, and stomach pain listed by four patients. Majority (25/37, 67.5%) of the patients who did not experience any side effects were on single therapy. Compliance was better among those who did not experience side effects- (26/37, (70.3%) compared with (10/19, 52.6%) who experienced side effects being compliant.

Most (38/56, 67.8%) patients had their drug administered by an adult who is either a parent or a member of the family. Compliance was better when a parent or caregiver administered the drug (c^2= 2.188; p>0.05). Differences in social class did not affect patients' level of compliance or non- compliance (c^2= 0.764; p>0.05).

Rate of Default and Reasons for Default:
Our participants had been attending the neurology clinic for a period of 6 months to 168 months (mean 87 months), average number of visits was 6 visits per year; a few patients had about 8 to 12 visits / year due to poor seizure control. Forty three percent (24/56) of the patients had defaulted follow up more than once since admission into the clinic; period of default was between 3 months and 4 years; 71% continued treatment at home while 29% discontinued treatment.

Reasons for default were domestic such as bereavement; caregiver being ill or having to take care of a sick relative; financial constraint; prolonged period of therapy and poor seizure control with feeling of hopelessness, preference for spiritual healing. Three defaulted because seizures were controlled within the period.

Significant positive attitude changes were noticed following education of the patients and their families. On follow up one month after enrollment into this study, compliance improved from 64.3% to 87.5% based on patients taking > 85% of medication prescribed.[19] Most of the parents/caregivers (96.4%) were satisfied with the level of care being received at the clinic.

DISCUSSION

Epilepsy is a common chronic neurological disorder of childhood in our setting with generalized tonic clonic epilepsy being the most frequent type observed in the current study. Similar studies have been reported in Nigeria where the generalized tonic clonic form of epilepsy constitutes about 25 to 65% of the cases studied.[23]

The knowledge of the common cause / s of epilepsy was poor among the caregivers of the children in the current study. Evil spirit and supernatural powers were believed to be the cause of epilepsy in about 5.4% of them. This compares favourably with findings from other authors who documented a strong belief that epilepsy was caused by these forces.[7,9]

This belief is reflected in the health seeking behavior of the parents/caregivers. In this study, 46.4% sought orthodox treatment at secondary health facilities (private hospitals) before presentation to our clinic which is a tertiary center. More than 30% sought different complementary and alternative (CAM) treatment before presentation including herbal medication and prayers while 17.9% did not seek any form of treatment probably out of ignorance of the disease and its treatment or for fear of stigmatization. These findings have been corroborated by other workers.[7] Half of the patients studied by Sureka and Sureka[7] had tried alternative treatments before presentation to the clinic.

Poor compliance was a serious problem among our patients. Consistent with other studies[5,24] a significant proportion (35.7%) of the children in the current study was not compliant to treatment. Epilepsy sufferers become non adherent or discontinue treatment due to several socioeconomic factors and suffer from seizures repeatedly.[6,9] Factors that affected level of treatment compliance among the patients studied were high cost of drugs; long period of treatment; multiple medications and associated side effects. The out- of-pocket expenses for patients with epilepsy in many developing countries are quite enormous due to lack of well established health insurance scheme and lack of adequate social security structure.[25,26] In Nigeria, the national health insurance scheme established about 10 years ago is still not universal as only workers in federal and a few state and organized private sectors are currently accessing its services. Most (94.6%) of the children studied had no form of health insurance and their parents had to pay for their treatment (consultation, drugs, investigation and so on) from

their pockets. Lagunju et al[27] also documented that 94.4% of the children studied had no form of health insurance and more than half of the families expended over 20% of their total family income on the care of the child with epilepsy. Institution of a well organized health insurance scheme in Nigeria will go a long way in reducing the cost of treatment of epilepsy among our children.

Consistent with other studies,[27, 28] compliance was better with single therapy than poly therapy. Leppik[27] noted that non- compliance increased with multiple medications when patients misunderstood instructions for using prescribed medications. Majority of our patients on single therapy had better seizure control than those on poly-therapy (79.4% compared with 27.2%). It has been documented that 60-80% of patients with epilepsy can be well controlled with one appropriately chosen drug.[28] However, a few of the patients with poor seizure control may require additional AED drug to achieve good control.

Some of the patients (35%) reported forgetfulness as their reason for poor compliance. The issue is whether the number of medications the patient needed to take indirectly determines his level of commitment to take them. Cramer and colleagues[29] argued that the number of medications was not a factor affecting adherence because once a patient remembered he was due to take a dose, he took them all at the same time. On the other hand, the number of daily doses also affected compliance. Patients with less frequent doses complied better than those with multiple doses of drugs. About 76.2% of our patients on twice daily dosing were compliant while only 28.6% of those on three times daily dosing were compliant. Adherence rates have been noted to be significantly higher in patients using less frequently dosed medication.[30] Cramer et al[31] observed that the number of daily doses was the most consistent predictor of non- compliance with AED treatment and an increased risk of seizure; and the odds of missing a dose increased by 27% each additional time a drug was expected to be taken.[32] In order to solve this problem, use of sustained-release (SR) formulations that enable once or twice daily dosing and have additional advantage of giving fewer side effects have been advocated[33]

The most common side effect noted among the participants in the current study was excessive sleep. Similarly, Martins et al[34] documented sleepiness as the most frequent side effect among their patients. Compliance was more among those that did not experience any form of side effect; 67.6% of them were on single therapy. Brodie[35] also noted that the likelihood of toxic effects, especially cognitive dysfunction, increased with the number of AEDs prescribed. Improved compliance and reduction in the number of patients with intolerable side effect from 15% to 9% were observed when the number of patients on poly-therapy was reduced from 60% to 45% in an Indian study.[7] Thus, it is important to balance adequacy of seizure control with the patient's quality of life.

Differences in social class did not affect our patients' level of compliance or non- compliance as more of the compliant as well as non -compliant patients were from low socioeconomic class contrary to the study that linked poor compliance with low socioeconomic status on one hand;[36] and another with high socioeconomic status.[37]

The average number of visits per patient was 6 visits per year. Gopinath and colleagues[38] observed that both the number of visits and effective communication between the doctor and the patient promoted adherence as multiple visits to the doctor enhanced communication and better compliance behavior among their patients. Level of care was not a contributory factor to poor compliance in our patients as most (96.4%) of the participants in this study were satisfied with the level of care being received at the clinic. Parent and child satisfaction with medical care has a positive influence on patients' adherence to treatment.[39,40]

Forty three percent of the patients studied had defaulted to follow up more than once since admission into the clinic with periods of default ranging between 3 months and 4 years; 29% of them did not continue medication as prescribed during the period of default. Similarly, Sureka and Sureka[7] noted that 37% of their patients did not attend the clinic regularly. Reasons for default in our patients were domestic: bereavement; caregiver being ill or having to take care of a sick relative; financial constraint; prolonged period of therapy and poor seizure control; faith in spiritual healing; and periods of symptomatic remission. This finding have been corroborated by other workers.[9, 12] Significant positive attitude changes were noticed following education of the patients and their families. Compliance improved from 64.3% to 87.5% based on patient / parent reported adherence and pill counting. Sureka and Sureka[7] also reported that the number of patients who missed their medication was reduced by half following education of patients and their families.

CONCLUSION

Poor compliance to medication is a major problem among children with epilepsy in our setting. The cost, number, frequency of dosing, and side effects of medications remain important factors that determine

level of compliance. In evaluating the effectiveness of treatment, the paediatrician needs to take all these factors into consideration.

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