Research Article

Determinants of Adherence to Anticonvulsants Therapy among Outpatient Epileptic Children in a Kenyan Referral Hospital

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Background: Epilepsy is a chronic disease requiring prolonged adherence to treatment. Adherence to anticonvulsants by epileptic children is important as studies have shown that about two-thirds of epileptic children can be completely freed from seizure if they persistently adhere to treatment for a period of 2-5 years. Conversely, non-adherence to anticonvulsants may lead to increased frequencies of status epilepticus and sudden unexplained death from epilepsy. There is scant literature on factors impacting on the adherence to anticonvulsants among children.

Objectives: To determine rate of adherence and parents/caregivers' factors influencing adherence to anticonvulsants among outpatient epileptic children attending neurology clinic.

Methods: Cross-sectional study design was carried out at Kenyatta National Hospital from May to July 2014. Systematic sampling was used to recruit a sample of 176 parents/guardians of children with epilepsy. Predesigned questionnaires and Morisky tool for assessing medication adherence were used to capture participant's socio-demographics and factors impacting on adherence to antiepileptics. Data were analysed using STATA software version 10. Discrete variables were summarized with frequencies and percentages while continuous variables were summarized using measures of central tendency and dispersion.

Results: The rates of adherence, when classified in terms of high, medium and low, were 36.9 %, 39.8 % and 23.3 %, respectively. Adherence rate was associated with parents/guardian marital status (Adjusted OR= 5.72, 95% CI= (1.50, 21.78), p=0.01) and education level (Adjusted OR=5.16, 95% CI= (1.88, 14.02), p< 0.01). Unavailability and inaccessibility of drugs were also shown to influence adherence.

Conclusion: Adherence to antiepileptic medication was poor. This was partly due to parents/guardian's related factors. Health care workers should explore ways and means of minimising these factors to improve on adherence.

Key words: Adherence, anticonvulsants, epilepsy, children.

1. Introduction

Epilepsy is a brain disorder characterized by recurrent and unpredictable seizures (Fisher et al, 2005; Shorvon, 2011). It is estimated that over 50 million people have epilepsy worldwide and 80 % of them are found in developing countries (Ndoye et al, 2005; Birbeck et al, 2007). In Africa the mean prevalence is 15 per 1000 (Sankar 2004; Chabi 2010). In Kenya, epilepsy is ranked the 37th leading cause of death (Diop et al, 2003; Mbuba et al, 2009). Although the disease onset can be at any age, majority of patients start suffering from childhood (Chabi, 2010; Carter et al, 2012).

Studies have shown that more children (70 %) than adults (60 %) can be completely liberated from epileptic seizure attack for many years after they completely adhere to treatment protocol for a period of 2-5 years (Amolo, 2011; Liu et al 2013). In epileptic patients non-adherence behaviour has been associated with increased morbidity and mortality along with increased time of hospitalization and the overall cost of treatment. The worst consequences of non adherence to anticonvulsants are increased frequencies of status epilepticus and sudden unexplained death from epilepsy (Jones et al, 2006). Consequently, better response and outcome from use of anticonvulsants depend on good adherence to prescribed drug.

Adherence has been regarded as a good determinant for intended clinical response (Hovinga et al 2008). Patients are expected to change their pre-treatment behaviour in favour of adherence. This depends on motivation on treatment, value of illness, age and desire to come out of the condition (Asadi-Pooya, 2005). However, complete adherence may be difficult to achieve as adherence is influenced by many factors including socioeconomic, patient disease, physician-patient relationship and in children, care giver related factors (Amolo, 2011).

Anticonvulsants are the main drugs in the management of epilepsy. Their wide range of side effects, drug interactions and individual response differences contribute to non-adherence (Gaitatzis and Sander, 2013). Most of the patients do not adhere to treatment due to misconceptions about the cause of the disease and affordability of medication (Amolo, 2011; Faught, 2012). Adherence in children is indeed a challenge because; their health decisions and choices are made by their parents/guardians (Amolo, 2011).

Many studies on adherence to medication have used Morisky tool to assess adherence. This tool is specially designed and validated questionnaire which can be modified to capture information from the study participants on the rate of adherence (Egede et al; 2008). The scale of adherence is measured depending on the scores resulting after calculation, in which score greater than 2 is regarded as low adherence,1-2 is medium adherence and 0 is high adherence (Morisk et al; 1986)

The main aim of this study was to determine the rate of adherence to anticonvulsants among outpatient epileptic children attending neurology clinic at Kenyatta National Hospital (KNH) and also to determine parents/guardian's related factors influencing adherence.

2. Methodology

2.1 Study design, site and population

This was a cross sectional study conducted on paediatric patients attending neurology clinic at the Kenyatta National Hospital, the largest referral and teaching hospital in Kenya.

2.2 Study population and eligibility criteria

Parents/guardians of children with epilepsy aged between 2-12 years and attending neurology clinic at the hospital from May to July 2014 were included. Parents/guardians who declined to give informed consent were excluded from the study.

2.3 Sample size and sampling procedure

The sample size was calculated using Fischer's formula using the estimated prevalence of 14.7 % which was the estimated prevalence rate of non-adherence to anticonvulsants among epileptic children at Kenyatta National Hospital (Amolo, 2011).

Systematic random sampling was used to select participants for the study in which every second parent/guardian coming from the consultation office was approached for enrolment. A total of 176 parents/guardians were recruited.

2.4 Data collection.

Morisk tool was used for assessing medication adherence among the children. This is a 6 items questionnaire which gave the scale of adherence to medication into >2 low adherence, 1-2 medium adherence and 0 high adherence. This is one of the most widely used validated tools for assessing medication adherence and has been used in various studies including World Health Organisation published studies of adherence (Morisky et al, 1986). Parents/guardians factors impacting on adherence were assessed using a predesigned and serialized study questionnaire. Serialization was done to avoid duplication of the results.

2.5 Data Management and analysis

Data obtained was coded, entered into a password protected Microsoft Access (2007) to create a database. It was then exported to STATA version 10 for analysis.

The rate of adherence was estimated using frequencies and percentages. Logistic regression was used in multivariable analysis to determine the presence of association between parent/guardian factors and adherence. Adjustment for confounders and effect modifiers was done to determine independence in the relationship between independent and dependent variables. This was achieved using binary stepwise backward multinomial logistic regression. P-value was set at 0.05 and any values with $p < 0.05$ were termed statistically significant.

2.6 Ethical considerations

Ethical approval to carry out the study was obtained from Kenyatta National Hospital/University of Nairobi

Ethics and Research Committee (KNH/UoN ERC) and letter (Ref No KNH-ERC/A/126) was given.

3. Results

### 3.1 Baseline characteristics of the study patients and parents/guardians

There was male preponderance at 62.5 %, with majority being in 4-5 years category. The participant median age was 6 years with an interquartile range (IQR) of 4-9 years.

Majority of patient's parents/guardians were females (72.8 %). The median age was 33 (IQR was 29-39) years. Most of parents were married (78 %) and (70 %) had attained secondary education as the highest level of education.

About (40 %) were unemployed, (29 %) were in employment and 16.5 % were casual labourers. About 50 % of parents/care givers had an average monthly income of Ksh 10,000. These characteristics are summarized in **Table 1**.

Table 1: Baseline characteristics of parents/guardians

Variable	n	Frequency
Married parent/guardians	137	78
Parent/guardians with secondary education	123	70
Unemployed parent/guardians	70	40
Family average monthly income of Ksh 10,000	88	10,00
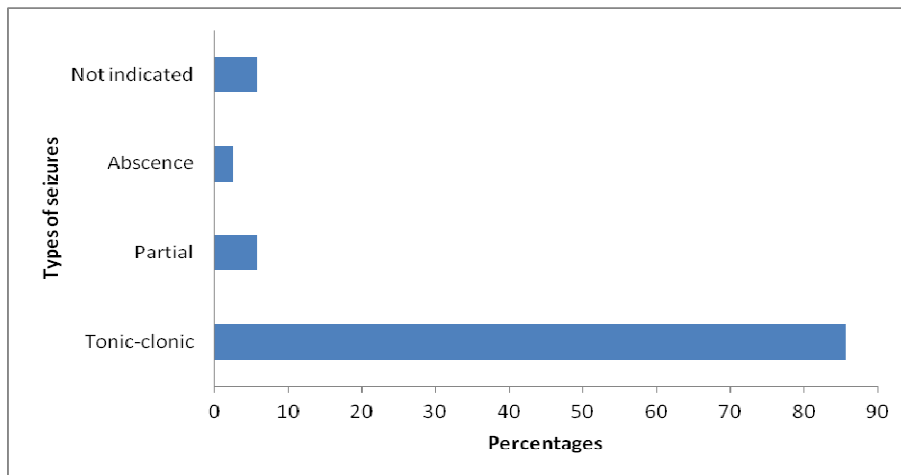
Figure 2: Prevalence of types of seizures
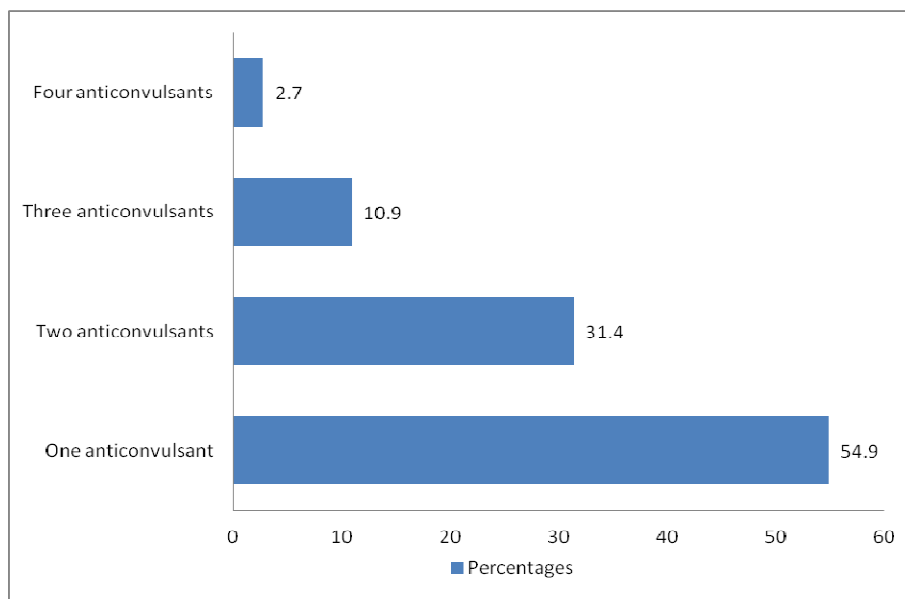
Figure 3: Prevalence of use of various anticonvulsants combinations

3.2 Types of seizures, anticonvulsants and regimens used at the neurology clinic

Majority of patients who participated in this study had tonic-clonic seizure (85.7 %) (**Figure 1**).

All epileptic children who participated in this study were on anticonvulsants. The types of monotherapy anticonvulsants and frequencies at which they were used were phenytoin 2%, Phenobarbital 49 %, Sodium valproate 24 %, Carbamazepine 21 %. The most used combinations were Phenobarbital/Sodium valproate 23 %, Carbamazepine/Sodium valproate/Phenobarbital 9 % and Carbamazepine /Sodium valproate /Phenobarbital/Clonazepam 3 % for two, three and four drugs, respectively (**Figure 2**).

3.3 Knowledge on Epilepsy by Parents/Guardians

On assessment of the knowledge on epilepsy, 65.3 % of the participants admitted having the requisite knowledge about the disease. Further, assessment on the parent/guardians knowledge on aetiology of epilepsy, curability, duration of treatment and side effects was also carried out. About two thirds of the parents /guardians knew that epilepsy is not a communicable disease. About 59 % responded that there is no cure while twenty one percent acknowledged that anticonvulsant treatment is lifelong. Twenty-four percent believed treatment for 6 months was adequate for complete cure. A large proportion (62.5 %) were not aware of the common the side effects associated with anticonvulsants.

3.4 Rate of Adherence to anticonvulsants therapy and Relationship between adherence to anticonvulsants therapy and baseline characteristics of the patient

Rate of adherence determination showed 36.9, 39.8 and 23.3 % of participants exhibited high, medium and low adherence levels. We determined adherence by age distribution and majority of highly adhering children (39.5 %) were aged between two and three years followed by those with age four to five years (38.7 %).

The last in this category were the school going children (35.3 %), aged six to twelve years. However, there was no statistically significant association between age groups of the patients and adherence level (p>0.05). The likelihood of adhering to anticonvulsant when the child in preschool years (4-5 years) was 0.97 times (95 % CI 0.42, 2.49) and 0.83 times (95 % CI 0.40, 1.74) in school years (6-12 years). The study findings revealed that adherence to anticonvulsants by children has no predilection to sex as there was no statistically significant association between adherence and sex of an epileptic child (p> 0.05). Nevertheless, being female child was associated with one and half times more likely to adhere to treatment compared to the male counterpart. (95% CI= 0.81, 2.89). These are summarized in **Table 2**.

3.6 Parents/Guardians Factors Influencing Adherence to Anticonvulsant Therapy

Because epilepsy is a chronic disease requiring persistently high adherence, the levels of adherence were categorised into two groups adhering (children with high adherence) and non-adhering (children with low and medium adherence) for the purpose of determination of associations between parent/guardian factors that impact on adherence to anticonvulsants and adherence levels.

There was a statistically significant association between the level of adherence and marital status (Adjusted OR= 5.72, 95 % CI= (1.50, 21.78) p=0.01) and level of education (OR=5.16 95 % CI= (1.88, 14.02) p< 0.01) of parent/guardian of an epileptic child. Parent's employment status and family average income was not statistically significantly associated with the rate of adherence to anticonvulsants by their children (p > 0.05) (**Table 3**).

The study observed a possible role of stigma on adherence with a minority (7.4 %) reporting not being comfortable to take their medication in the presence of friends or relatives. However, this factor was not statistically significant (p > 0.05).

Table 2: Relationship between adherence to anticonvulsants therapy and baseline characteristics of the patient

Variable	Medium and low adherence n (%)	High adherence n (%)	Bivariate OR	95% CI of OR	p- value
Age in years					
2-3	26 (60.5)	17 (39.5)	1	-	-
4-5	19 (61.3)	12 (38.7)	0.97	0.47,2.49	0.94
6-12	66 (64.7)	36 (35.3)	0.83	0.40,1.74	0.63
Gender					
Male	73 (66.4)	37 (33.6)	1	-	-
Female	36 (56.3)	28 (43.8)	**1.53**	0.81,2.89	0.19

Table 3: Relationship between adherence to anticonvulsants and sociodemographic characteristics of the primary care givers

Variable	Non adherence n (%)	Adherence n (%)	Crude OR	95% CI	P-value	Adjusted OR	95% CI	P-Value
Level of education								
Primary	40 (83.3)	8 (16.7)	1.00	-	-	1.00	- -	
Secondary	32 (48.5)	34 (51.5)	5.31	(2.16-13.06)	0.00	5.16	(1.88-14.02)	**0.001**
College	35 (61.4)	22 (38.6)	3.14	(1.24-7.95)	0.02	3.72	(1.86-10.92)	
None	3 (75.0)	1 (25.0)	1.67	(0.15-18.14)	0.68	1.67	(0.09-36.45)	
Marital status								
Single	24 (85.7)	4 (14.3)	1.00	-	-	1.00	- -	
Married	80 (58.8)	56 (41.2)	4.20	1.38-12.77	0.01	5.72	(1.50-21.78)	**0.01**
Divorced	0 (0.0)	1 (100.0)	-	-	-	-	-	
Widowed	3 (75.0)	1 (25.0)	2.00	(0.16-24.33)	0.59	4.76	(0.26-88.43)	
Separated	2 (50.0)	2 (50.0)	6.00	(0.65-55.66)	0.12	14.89	(1.12-197.74)	
Employment status								
Employed	33 (66.0)	17 (34.0)	1.00	-	-			
Unemployed	43 (61.4)	27 (38.6)	1.22	(0.57, 2.60)	0.61			
Casual labourer	16 (57.7)	12 (42.9)	1.46	(0.56, 3.76)	0.44			
Others	14 (60.9)	9 (39.1)	1.25	(0.45, 3.47)	0.67			
Family's average monthly income (Thousands in Kshs)								
0-5	25(71.4)	10(28.57)	1.00	-	-	1.00	-	**-**
6-10	32(65.3)	17(34.69)	2.39	0.52, 3.40	0.55	1.20	0.41, 3.48	0.74
11-20	22(51.1)	21(48.84)	2.92	0.93, 6.15	0.07	2.19	0.72, 6.71	0.17
21-30	6 (46.15)	7 (53.85)	2.92	0.78, 10.85	0.11	2.49	0.57, 10.77	0.22
31-40	6 (75.00)	2 (25.00)	0.83	0.14, 4.85	0.84	0.69	0.09, 4.71	0.70
41-50	2 (50.00)	2 (50.00)	2.50	0.31, 20.27	0.39	1.38	0.16, 12.09	0.77
>50	9 (75.00)	3 (25.00)	0.83	0.19, 3.73	0.82	0.60	0.74, 3.74	0.58

Table 4: Types of anticonvulsants available at the pharmacy

Type of anticonvulsant	Class	Regularity of availability	Formulations available
Phenobarbitone	Barbiturate	**Always**	Tablets
Phenytoin	Hydantoin	Sometimes	Injection, capsules
Carbamazepine	Carboxamide	**Always**	Tablet, syrup
Clonazepam	Benzodiazepines	**Always**	Tablets
Sodium valproate	Fatty acid derivative	Most times but not always	Tablets
Topiramate	Fructose derivatives	Not available	
Diazepam	Benzodiazepines	Not available	
Gabapentin	GABA analogs	Not available	
Lamotrigine	Phenyltriazine	Not available	
Lorazepam	Benzodiazepines	Not available	

3.7 Availability of Anticonvulsants at the Pharmacy

The pharmacy that serves the neurology clinic caters for fill and refill services of anticonvulsants. During the study period, assessment for availability of anticonvulsant at this pharmacy was done regularly during clinic days. Types of anticonvulsants, their formulations and the regularity of their availability were as shown in the **Table 4**.

4. Discussion

According to WHO and other studies, the successful outcomes of treatment of epilepsy with anticonvulsants depend on high adherence level (Asadi-Pooya, 2005; Faught, 2012). However, our study revealed that the rate of high adherence level was relatively low at 36.9 %. This suggested that control of seizure in the hospital was poor. Studies done in an adult epileptic clinic at KNH showed the rate of non-adherence to be 40 %, with many non-adhering patients exhibiting poor seizure control (Mativo, 2004; Amolo, 2011). Studies done in developed countries particularly USA showed that the rate of adherence in children with chronic diseases averages at 50 % (Modi et al, 2011). The rate of adherence in paediatric clinic in KNH was lower than that of adults in the same setting. (Mativo 2004; Amolo, 2011).

Previous studies done at the same hospital to determine levels of seizure control in children, suggested that the cause of poor control of seizure was due to non-adherence. Education level of parent/guardians was shown to be statistically significantly associated with adherence to anticonvulsants. Children with parents who had attained secondary level of education were 5.31 times more likely to adhere to anticonvulsants. Likewise children from a family whose primary care giver had attained college level of education were 3.14

times more likely to adhere to anticonvulsants. Perhaps these parents had sufficient information on the disease and importance of adherence. Education may improve the ability to interact with health care givers and ask relevant questions. The knowledge, attitude and practice of parents and guardians of children with epilepsy showed that the more the parent/guardian is informed the better the outcome. Studies have also revealed that provision of proper information and knowledge of a disease to the patient or primary care giver (Parent/guardian) leads to higher adherence to treatment protocols (Muasya et al, 2001).

Marital status of parents/guardian was also shown to influence adherence. A child receiving primary care from a married couple was 5.72 times more likely to adhere to anticonvulsants as compared to child being raised by a single parent. Another study on determinants of adherence to TB medication at KNH showed a similar association (Ongáyo et al, 2010). This may probably be due to the mutual social support that such married couples enjoyed in the care of a child. The possibility of influence of stigma on adherence in this study is in tandem with a study done in Zambia among epileptic patients where stigma was significantly associated with adherence ($p < 0.01$) (Birbeck et al, 2007, Hovinga et al, 2008). The fear of stigma can lead to fear of giving medication to a child until after friends or relatives have left.

Our study showed that non-adherence rate increase with the age of patients. Majority of non-adhering children were in higher age group. However, the association between rate of adherence and age of the patients was not statistically significant in bivariate analysis ($p > 0.05$). The difference could be due to decreased social cohesion between a parent/guardian and the child as a child grows older and become independent in some activities. A study done in Uganda on adherence to antiepileptic drugs among children

attending a tertiary health unit in a low resource setting found that occupation of a care giver influences adherence. Children receiving care from a primary care giver with very involving occupation were not likely to adhere to anticonvulsant therapy (Jones et al, 2006).

WHO suggests treatment of epilepsy with single anticonvulsant agent, and the second, third or fourth drug added gradually if symptoms are not under control. It also suggests the first line drug to be phenobarbital in developing countries because of its low cost. Our study found many patients were on single anticonvulsant agent most of whom were on phenobarbital followed by sodium valproate then carbamazepine and lastly phenytoin .The most commonly used combinations was phenobarbital and sodium valproate. The study done by Mativo et al in adult neurology clinic at KNH found most patient on monotherapy were on carbamazepine followed by phenytoin then phenobarbitone and lastly sodium valproate This study also pointed out that the most common combination regimen used was carbamazepine and phenytoin , used by a third of the patients (Muasya 2000; Mativo 2004).

Family average monthly income had no statistically significant association with adherence in our study. This was least expected based on the regularity of drug availability in the hospital. Patients would have been expected to purchase their anticonvulsants from unsubsidized pharmacies and consequently influencing adherence. Our study revealed that phenobarbitone, carbamazepine and clonazepam, were only anticonvulsants which were always available at the pharmacy. Phenytoin and sodium valproate were available in certain periods while other anticonvulsants were not available during the whole period of this study. Studies on adherence have singled out one of the causes of non-adherence to be lack of access to anticonvulsants because of cost and availability (Mativo 2004; Amolo 2011)

Gender of a patient had no statistical significant association with adherence to anticonvulsant therapy. A similar study done among adult patients in United Kingdom did not show an association between adherence rate and gender of a patient. Similar studies done in KNH at adult and paediatric clinics did not show the association between adherence to anticonvulsants or poor seizure control and gender (Amolo, 2011; Liu et al 2013).

Since children's health care is determined by the parents/care giver, it is important that these care givers routinely receive enough information on the disease, its treatment and importance of adherence from healthcare providers. Health care delivery system must also ensure availability and affordability of anticonvulsants to optimise adherence.

5. Conclusion

Less than 40 % of participants showed high adherence to anticonvulsant therapy. Unavailability and inaccessibility of drugs as well as parents/guardians socioeconomic factors were the major determinants of adherence to antiepileptic medication in children.

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