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PATTERNS OF ANTIEPILEPTIC DRUG USE AND SEIZURE CONTROL AMONG PEOPLE WITH EPILEPSY IN A SUBURBAN COMMUNITY IN SOUTHEAST NIGERIA

UTILISATION DES ANTIEPILEPTIQUES ET CONTROLE DES CRISES DANS UNE COMMUNAUTE D'UNE BANLIEUE DANS LE SUD-EST DU NIGERIA

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ABSTRACT

Background

Epilepsy is characterized by episodic and unpredictable seizure recurrences which are often amenable to medical treatment. Simple and readily available medications can be used to control seizures in epilepsy. However, in many communities in developing countries seizure control among people living with epilepsy is still poor.

Method

We assessed the patterns of antiepileptic drug use and seizure control among persons living with epilepsy in a suburban community in Southeast Nigeria found in a two phase cross-sectional study. Detailed information on epilepsy treatment, seizure control and patterns of antiepileptic drug use (AED) by those diagnosed with epilepsy was determined by use of a semi-structured interviewer administered questionnaire. Further verification of the type of antiepileptic drugs (AEDs) was done by drug inspection.

Result

The total of 29 cases of active epilepsy comprising 16 (55.2%) males and 13 (44.8%) females were found. Those receiving AEDs at the time of survey were 7 (24.1%), 11(37.9%) who had previously used AEDs had stopped and the remaining 11 (37.9%) were AEDs naïve. Carbamazepine monotherapy was used by 57.1% (n=4) while phenobarbitone was used by 42.9% (n=3). The antiepileptic drugs were prescribed in all these cases by medical personnel. Over 82% of the persons with active epilepsy found were having more than one seizure per month.

Conclusion

Active epilepsy was prevalent in this suburban community with only 24.1% (n=7) of them receiving treatment with AEDs. Seizure control was poor even among those receiving AEDs and carbamazepine monotherapy was most commonly used AEDs.

INTRODUCTION

Epilepsy is one of the world's most prevalent non-communicable diseases with about 80% of the estimated 50 million people living with epilepsy residing in developing countries (20). Epilepsy is characterized by episodic and unpredictable seizure recurrences and these results in immense psychosocial consequences for sufferers and relatives alike. Despite these consequences, the overall prognosis of epilepsy remains good. Often time epilepsy is amenable to medical management with simple and readily available medications.

The goal of treatment is to maintain a normal lifestyle by complete seizure control with minimal side effects. Treatment is with pharmacological and non pharmacological methods. Antiepileptic drug (AED) therapy is the mainstay of treatment for the majority of patients. The selection of an AED is based on efficacy against specific seizure types and the adverse effect profile. Non-pharmacological strategies are primarily reserved for drug-resistant epilepsy. If the seizures are provoked by external factors, for instance sleep deprivation or excessive alcohol, simple avoidance might be sufficient to prevent further attacks. AEDs are highly successful in suppressing seizures in most patients. With correct, early and uninterrupted therapy, up to 75% of patients with epilepsy eventually become seizure free, many of them within 5 years after diagnosis (3) while about 25% of patients may not respond to any kind of therapy (3).

AEDs differ in many important aspects including their efficacy against different seizure types, their side-effect profiles, their potential for pharmacokinetic interactions, and their ease of use. Several antiepileptic drugs exist, these include the older antiepileptic drugs generally regarded as ¡°old¡± or ¡°established¡± AEDs (carbamazepine, phenobarbitone, phenytoin, valproic acid, e.t.c) and the newer antiepileptic drugs (vigabatrin, lamotrigine, felbamate, gabapentin, topiramate, e.t.c). Except for a better side effect profile, there are no convincing data to show that newer drugs compared with older ones, achieve superior seizure control (3). Older AEDs have several advantages including long-term experience, lower cost and known efficacy. The AEDs most frequently prescribed in the developing world are phenobarbital and phenytoin, (6) they are the cheapest and are prescribed in 65-85% of cases (6).

Initiation of therapy for newly diagnosed patients is with a single antiepileptic drug. Combination therapy is recommended when two successive AEDs given as monotherapy have failed. Agents with a low risk of pharmacokinetic interactions are preferred for combination therapy and success of combination therapy can be improved by paying attention to mechanisms of action and using lower dosages (2). With correct, early and uninterrupted therapy, up to 75% of patients with epilepsy eventually become seizure free, many of them within 5 years after diagnosis (3). About 25% of patients may not respond to any kind of therapy. Antiepileptic drugs (AEDs) are highly successful in suppressing seizures in most patients.

MATERIAL AND METHODS

Study area: The study was conducted in Ukpo an Igbo speaking community in Southeast Nigeria. Ukpo is the headquarters of Dunukofia Local government area in Anambra State Nigeria. The population of Dunukofia local government according to the 2006 National population census report is 96,517 and it has 20,708 households by ownership status of dwelling units (11). The people of Ukpo are predominantly subsistent farmers and they also trade on farm produce. There are a few civil servants under the school system and the Local government employment. The major religion of the people is Christianity with few who are still adherents of Africa traditional religions. The people are acquainted with orthodox treatment since the establishment of a health clinic in the community in the Eastern region of Nigeria. This together with the advent of Christianity had not succeeded in modifying much of the cultural beliefs and practices about epilepsy. This health clinic came under the management of Nnamdi Azikiwe University Teaching Hospital (NAUTH) in 1997 and it became a centre for medical student training in community medicine and recently has become the epicenter of the Neuro-epidemiology and Community Neurology centre of the Neurology unit of the Department of Medicine, Nnamdi Azikiwe University. In addition there is another health centre and two maternity homes and a handful of patent medicine stores in the community but no pharmacy store. Drugs are sourced from these patent medicine stores or the pharmacy sections of the health centers and from pharmacies in neighboring communities.

THE SURVEY

The study was a two phase cross-sectional descriptive study. The first phase was preceded by a census of households. Household interviewed were selected using computer generated random numbers. Every member of a selected household was interviewed. A total of 6800 persons from 1700 households in the community were selected and interviewed in the first phase taking into consideration the design effects and epilepsy prevalence.

The first phase of the study was a door-to-door using a modified version of the WHO protocol (15) for detecting the presence of neurological diseases in the community which was forth and back translated into the local vernacular of the community. This protocol was validated in the area and found to have a sensitivity of 100% and specificity of 65% for active epilepsy. In the second phase all those identified as possibly having epilepsy were evaluated by neurologists and senior residents in neurology. Epilepsy was diagnosed based on the ILAE guidelines (9) and electroencephalogram (EEG) was done in for 19 (65.5%) of the persons with active epilepsy. Detailed information on epilepsy treatment, seizure control and patterns of antiepileptic drug use was determined by use of a semi-structured interviewer administered questionnaire. Further verification of the type of AEDs was done by drug inspection.

Ethical approval for the study was obtained from the Ethical Committee of the Nnamdi Azikiwe University Teaching hospital Nnewi and permission to conduct the study from the Ministry of Health Anambra State, Nigeria. Informed consent was obtained from the traditional ruler and his council, from household heads and adults subjects and from parents or close family relatives of children. All the subjects gave their consent. Parents or close family members acted as proxy for Children and persons unable to understand and respond to the questions during all the phases of the survey.

STATISTICAL ANALYSIS

Data collected was entered into the research instrument and confidentiality maintained. Data collected was analyzed using Statistical Package for the Social Sciences SPSS version 15 (SPSS Chicago Inc., IL, USA). Prevalence values with their 95% confidence intervals were calculated, relevant percentages, frequencies, means and standard deviation were calculated. Fisher's exact test was used to compare percentages where necessary. Findings were represented with relevant tables.

LIMITATIONS

The analysis of antiepileptic drug use was restricted to those on AEDs at the time of survey whose drug type and dosage regimen were verifiable.

RESULT

In the first phase of the study 6800 persons were screened that included 3249 (47.8%) males and 3551 (52.2%) females. Seventy six persons were identified at the first phase as possibly having epilepsy. At the second phase 29 persons were found to have active epilepsy giving a prevalence of 4.3 per 1,000 (95% CI: 2.7 - 5.9). The identifiable seizure types on clinical assessment were generalized seizures 62.1% (n=18) and partial seizures 37.9% (n=11).

The patterns of AEDs use is shown in Table 1. At the time of study 24.1% (n=7) of the persons with active epilepsy were receiving AEDs, while 37.9% (n=11) of the persons with active epilepsy who had previously use AEDs had stopped. The remaining 37.9% (n=11) had never been treated with AEDs. AEDs monotherapy was used by all the subjects (100.0%) still receiving AEDs at the time of survey and these were prescribed by medical staffs (medical doctors). Carbamazepine was used by 57.1% (n=4) and phenobarbitone by 42.9% (n=3) of the persons with active epilepsy.

The duration of seizures and seizure frequency are shown in Table 2. The mean duration of seizures for patients with active seizure was 6.07 ± 4.6 years. The duration of seizure was 5 years or less for 58.6% (n=17) of the persons with active epilepsy. The seizure frequency was more than one seizure episode per month for 82.8% (n=24) of cases of active epilepsy and less than one seizure episode per month for the remaining 17.2% (n=5). There was no statistically significant difference (P>0.05) in seizure episodes

between those on AEDs and those not receiving AEDs (Table 3), this also applied to the difference in seizure types and the type of antiepileptic drug prescribed (Table 4).

DISCUSSION

Epilepsy one of the most common chronic neurologic diseases the world over is amenable to medical treatment. This study concerned a population sample representative of the Ukpo community in Dunukofia local government area of Anambra state Nigeria. The prevalence rate of 4.3 per 1,000 (95% CI 2.7-5.9) found in this present study was lower than 5.3/1000 and 37/1000 reported by Osuntokun et al (14, 15) in Igbo-ora and Aiyete Southwest Nigeria respectively and 6.2/1000 by Longe and Osuntokun (10) in Udo Southsouth Nigeria. However Osuntokun et al (14) had acknowledged that the existence of health facilities in Igbo-Ora would have contributed to the lower prevalence of epilepsy in Igbo-ora compared to Aiyete which was only 20KM away. The established health care facilities spanning for over more than four decades now in Ukpo might account for the low prevalence in this present study. Furthermore the point in time of this study and difference in the definition of active epilepsy between the present study and that of Osuntokun et al (14) might also be contributory.

Simple and readily available medications can be used to control seizures in epilepsy. Up to seventy five percent of patients with epilepsy will eventually become seizure free within 5 years of diagnosis (3) while about 25% of patients may not respond to any kind of therapy (3). In our study the percentage of persons with active epilepsy using antiepileptic drugs at the time of survey was 24.1% (n=7). This is comparable to 27.5% found by Aziz et al (1) in Urban Pakistan. However at Igbo-ora a suburban community that is comparable to Ukpo, Osuntokun et al (14) reported that 4% (n=4/101) were not on AEDs. This was about three decades ago. During door to door surveys the percentage of persons with active epilepsy on AEDs had varied between studies conducted in the developing countries and between communities within the same country. In a community study in Turkey, Aziz et al (1) found that 30% of the epileptic population was on AEDs. The percentage of people living with epilepsy (PWE) on AEDs is less in studies conducted in rural communities. Aziz et al (1) reported 1.9% in rural Pakistan while Dent et al (5) reported 4.2% in a rural community in Southern Tanzania.

The AEDs that the patients were using at the time of the study were carbamazepine (57.1%) and phenobarbitone (42.9%). Prior to the study, three persons had used phenytoin. Phenobarbitone and/or phenytoin were used by the persons with epilepsy found by Osuntokun et al (14) at Igbo-ora and Dent et al (5) in Southern Tanzania. Phenobarbitone has been successfully used to treat epilepsy by primary health workers in rural Africa (21). Phenobarbitone is recommended by the World Health Organization (WHO) as the drug of choice for management of seizures in developing countries (8). Previous studies had noted phenobarbitone and phenytoin to be the most often prescribed AEDs in the developing world, the two drugs being the cheapest were prescribed in 65-85% of treated epileptic patients (6). In a study, Ogunniyi et al (12) in a hospital series at Ibadan in 1998 found that phenobarbitone was the single most commonly prescribed antiepileptic agent during that period.

The World Health Organization reported carbamazepine as the third most prescribed AED in developing countries and is prescribed for only 5 to 20% of cases (6). However, the use of carbamazepine is gaining acceptance due to its favorable anticonvulsant efficacy and supplementary psychotropic use (13) and this might in part explain the high use of carbamazepine found in our study. This is further supported by a recent finding in a study conducted in Ilorin, Nigeria by Sanya and Musa (17) on private practitioners' perspective of epilepsy management that 64.8% of the respondents prescribed carbamazepine, while 25.4% and 14.1% prescribed phenobarbitone and phenytoin respectively. Antiepileptic drug monotherapy was used by all the patients in this study who were still on AEDs at the time of survey. This is encouraging as monotherapy should be the aim for most people with epilepsy (19). Optimum seizure control can be obtained with a single drug for between 70% and 80% of patients (18, 19).

The frequency of seizure was high among the PWE in our study. The majority of those with active epilepsy (82.8%) had more than one seizure episode per month. There was no statistically significant difference between the episodes of seizures in those using AEDs and those not receiving AEDs at the time of survey. Though the number of persons in this study that were on AEDs was few to make reasonable conclusions, various factors which may be patient related or health care related however, are known to contribute to poor seizure control in epilepsy. The major health care related problem identified in our study was under dosage. The patients in our study on AEDs at the time of the survey were grossly under dosed. The maximum dosages of the drugs were carbamazepine 200mg daily (plain not controlled release formulation) and

phenobarbitone 60mg daily despite continuing seizures. Antiepileptic drugs are highly successful in suppressing seizures in most patients and with probable adequate dosing and education of both the patients and health care providers in this community epilepsy control will be improved. Another health care related factor that may have also contributed to the poor seizure control was the choice of antiepileptic drug used. Carbamazepine was used for three patients we found to be having primarily generalized seizure based on clinical assessment using the ILAE guidelines.

Self withdrawal from AED therapy was high in our study. We found that 37.9% (n=11) of the persons with active epilepsy had used AEDs previously but had stopped at the time of study. This is higher than 27% reported by Aziz et al (1) in a mixed rural and urban community in Turkey. The major reason found in this study to be responsible for permanently discontinuing AEDs was patients' dissatisfaction arising from the continuity of the seizures despite the use of AEDs. Other workers have also reported in the past that the majority of patients who permanently discontinue their antiepileptic medication do so of their own accord (4, 7). About one-third (37.9%) of the persons with active epilepsy in our study had never used antiepileptic drugs, this is similar to other reports were up to one-third of the epileptic population were never on medication (16).

CONCLUSION

Active epilepsy was prevalent in this suburban community in Southeast Nigeria. Among the PWE less than one third were receiving treatment with AEDs. Seizure frequency has high even among those receiving AEDs. More than a quarter of the PWE had never been treated with antiepileptic while more than half of those who were started on antiepileptic drug have discontinued of their own accord despite continuing fits.

Table 1 Patterns of Use of Antiepileptic Drugs

Characteristics	Number of subjects	Percentage
Use of AED		
Number with active epilepsy	29	100.0
Number receiving AED at time of survey	7	24.1
Number that had previously used AED(s)	11	37.9
Number that never used AED(s)	11	37.9
AED regimen		
Monotherapy	7	100.0
Polytherapy	0	0.0
Type of AED (a)		
Phenobarbitone	4	42.9
Carbamazepine	3	57.1

(a) Analysis limited to those using AEDs at time of survey because of problems of recall. However three patients with active epilepsy had used phenytoin before the time of survey.

Table 2 Seizure duration and control

Characteristics	Number	Percentage
Duration of seizures		
<5 years	17	58.6
6-10 years	8	27.6
> 10 years	4	13.8
Total	29	100.0
Mean duration of seizures	6.07 ± 4.6	
Frequency of seizures (a)		
≤ 1 per month	5	17.2
>1 per month	24	82.8
Total	29	100.0

(a) Seizure frequency the year prior to survey

Table 3 Seizure frequency and Antiepileptic drug (AEDs).

Seizure Frequency	On AEDs (%)	Not on AEDs (%)	Total (%)
≤ 1 per month	1 (3.4)	4 (13.8)	5 (17.2)
>1 per month	6 (20.7)	18 (62.1)	24 (82.8)
Total	7(24.1)	22 (75.9)	29 (100.0)

Fisher's exact test (2-sided) P =1.0

Table 4 Seizure type and type of antiepileptic drug prescribed

Seizure Frequency	Carbamazepine (%)	Phenobarbitone (%)	Total (%)
Generalized	3 (42.9)	3 (42.9)	6 (85.7)
Partial	1 (14.3)	0 (0)	1 (14.3)
Total	4 (57.1)	3 (42.9)	7 (100.0)

Fisher's exact test (2-sided) P =1.0

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