Original Research Article

The effect of quality of life, medication adherence and number of medications on patients with epilepsy

Wednesday J Edefo [1]* and Penaere T Osahon[2]

[1]Department of Pharmacy, Federal Neuropsychiatric Hospital, PMB 1108, Benin City, 300001, Nigeria. [2]Departments of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy, University of Benin, PMB 1154, Benin City, 300001, Nigeria.

* For correspondence: *Email: edefojoshua2000@yahoo.com, Tel: 2347035800341*

Abstract

Purpose: In the management of people with epilepsy the effect of variables such as of quality of life, medication adherence, and number of antiepileptic drugs on seizure control are veritable tools to optimize their care thus the study aimed to assess the correlation and relationship of quality of life, medication adherence, and number of medications on seizure control.

Methods: This was a cross-sectional study of sample size of 141 respondents using systematic sampling techniques. Frequency of seizures was gotten from self-developed proforma. Adherence was evaluated using the Modified Morisky Adherence Scale (MMAS) instrument while Quality of life was evaluated using Quality of Life in Epilepsy Patient Weighted-10 questionnaire (QOLIE-10P) instrument. Correlation analysis was used to determine if these variables were related while multiple regression analysis was done to determine the extent these variables were related.

Results: Seizure control and quality of life, seizure control and medication adherence, and that of seizure control and number of medications taken by the patient were related with a p value of <0.001, <0.001, 0.017 respectively. Multiple regression of the combined effects of quality of life, medication adherence, and number of medication as explanatory variables on seizure control gave coefficient (R), adjusted R^2 and standard error of estimate as 0.979, 0.956, 0.632 respectively while each of the variable has effect on reduction of seizure episodes as -0.076, 0. 925, 0.176 respectively.

Conclusion: Quality of life, medication adherence, and number of medications are related with seizure control; these variables have combined effect of more than nine-tenth on variability of seizure control while their individual effects are at least one-tenth on alteration of frequency of seizure episode.

Keyword: Seizure-control, quality-of-life, medication-Adherence, epilepsy

Introduction

Epilepsy can be referred to as unprovoked excessive neuronal electrical impulses leading to seizure which may alter consciousness and can manifest as starring and loss of physical balance. The consequences of epilepsy can be quite severe and include excessive bodily injury, neuropsychological and psychiatric impairment, social disability and shortened lifespan with mortality rates of 2 to 4 times higher in people with epilepsy than in general population [1,2].

Management of epilepsy can be achieved through pharmacotherapy. Medications used in the treatment of epilepsy include sodium valproate, carbamazepine, phenytoin, gabapentin, ethiosuximide, diazepam and these drugs are called antiepileptic medication. Epilepsy has been shown to be successful

managed with antiepileptic medications and adherence to these medications has resulted into seizure control [3].

It has been controversial in some researches whether adherence to antiepileptic medication reduces number of seizure episodes as there are individuals (about 10%) who do not adhere to medication and do not experience seizures and vice versa, this has been a source of frustration to health care professionals and patient alike [4]. Another study depicted that patients may not perceive non-adherence as the main attributing factor in seizures control, when patients were asked if anything increased the likelihood of a seizure, two quarter of the respondents opted for stress or emotion, one-fifth had fatigue, and only about one-tenth stated inadequate medication adherence [5].

In addition, quality of life had been shown to be highly related to seizure control in different studies [5-6] conducted in United States of America and India. Study done showed that about one-third of the respondents who participated had low quality of life and more of these persons were those who had poor seizure control. In another study, data showed that non-adherence had strong relationship with low scores in quality of life (QOL) measurements and decrease in work productivity [1].

Despite several researches on patients with epilepsy, there has been very limited related studies done in Nigeria such as research on medication adherence and adverse effect profile of antiepileptic drugs [7] and such studies did not fully addressed the controversy surrounding the impact of medication adherence on seizure control thus the objectives of this study which were aimed to determine the correlation of quality of life, medication adherence, number of medication on seizure control and to assess the relationship of quality of life, medication adherence, number of medication on seizure control.

Methods

Setting

The study was conducted at Federal Neuro-Psychiatric Hospital, Benin City, Edo State, Nigeria which is a tertiary hospital. The hospital has 228-bed capacity as at 27th February, 2014 and serves the people living in the south-south zone of Nigeria. Various health professionals such as pharmacists, physicians, nurses, psychologists, health administrators are employed in the institution.

Ethical approval

Ethical approval was obtained from the Medical Research and Ethics Committee of the hospital with reference No: PH/A. 864/134. Recruitment of participants was on voluntary basis and devoid of fraud or undue influence. The content of the consent form was clearly read out and explained to each patient and/or patient's caregiver, and they were given opportunity to ask questions. Interpreters were used to clearly explain the content of the consent form to any illiterate participants. Anything not clear to the participants or caregivers was further explained. Only participants who accept to freely give consent were included to participate in the study. Those who did not give their consent to participate were not included in the study, and their nonpartisan did not affect the health care attention or services given to them. All participants were assured of the confidentiality of the information provided. The consent form was signed by each participant recruited or caregiver who clearly understood its content.

Study design/sample size determination

It was a cross sectional design using systematic sampling interval of two and where the patients refused to participate, the next person in line is taken. Sampling determination was determined using the formula [8], n = N/1+N (e2) where N (population) = (224) as at 27th February, 2014, e (precision) = (0.05), n (sample size), which gave approximately a sample size of 140.

Inclusion and exclusion criteria

Patients on out-patient basis, above 18 years diagnosed for epilepsy by psychiatrist, receiving antiepileptic medication(s), have had regular treatment in the setting for at least 6 months with stable doses of antiepileptic drugs and gave informed consent were eligible. Patients with epilepsy who were prescribed other medications for other conditions alongside their antiepileptic medications were excluded.

Data collection

Questionnaire was used in the study with four sections A to D. Section A of the questionnaire

is a self-developed instrument for assessing socio-demographic characteristics of patients. Section B instrument was used to determine seizure control for the past 4 weeks from the day the data was collected. The names of the medications used were sodium valproate, carbamazepine and folic acid.

The quality of life was assessed using a validated instrument, Patient Weighted Quality of Life in Epilepsy -10 instrument (QOLIE-10-P) [9] in section C of the questionnaire. The instrument contains 10 items and 1 question on level of distress caused by epilepsy. The instrument is divided into three main factors; epilepsy effects (mental, physical and memory effects), mental health (energy, depression and quality of life) and function (seizure worry, driving, work and social limitation).

Patient adherence and persistence in long term continuation of treatment was assessed using another validated instrument, the Modified Morisky Adherence Scale (MMAS) instrument in section D of the questionnaire [8]. Pretesting was carried out in all the validated instruments used in this study.

Method of data analysis

The collected data were entered into Microsoft Excel (Microsoft Corporation, Redmond, Washington), sorted and checked for accuracy and analyzed to give descriptive statistics while inferential statistics was done using Statistical Package for the Social sciences (SPSS) statistical software, IBM, version 22 (SPSS Incorporation; 233 south Walker Drive Chicago IL).

Epileptic seizures control since the past 4 weeks was determined by numerical count of the number of seizures episodes under the period review, starting from the number of epileptic seizure 1 week ago, 2 weeks ago, 3 weeks ago and finally 4 weeks ago. A total count of all the (1-4) weeks was recorded and used to measure seizure control as the lower the value, the better the seizure control. The number of different type

of medications the respondent were on to control the epileptic seizure were also computed.

Quality of Life in Epilepsy (QOLIE-10-P) is a 11-item questionnaire on a 5 point likert scale in most of the items. The total score was the sum of scores for all questions divided by the number of items answered. The lower the QOLIE-10P value, the higher the quality of life while the higher the value the lower the quality of life of people living with epilepsy.

The Modified Morisky Adherence Scale (MMAS) assesses adherence to medications in long term treatment. The scale contains a total of 6 questions with a maximum score of 6, 3 questions attributed to motivation and another 3 attributed to knowledge of medication. Each question was given a score of 1 for 'no' and 0 for 'yes'. Questions on motivation levels assess forgetfulness and carelessness as indicators. On the other hand, questions on knowledge of medication evaluate management of medications such as stopping of medications and understanding the long-term benefits of continued therapy. This provides a score range of 0 - 3 for both motivation level as well as medication knowledge. The higher the total score of the scale of an individual the better the adherence of such an individual to the medication being taken while the lower the scale, the lower the possibility of medication adherence.

Correlation analysis of epileptic seizure control and quality of life, seizure control and medication adherence, seizure control and number of medications taken was conducted. Analysis of variance to test for significant difference between group means of variables was done and multiple regression analysis was also carried out where seizure control is the dependent variable while quality of life, medication adherence and number of medications taken are the explanatory variables. A p-value of less than or equal to 0.05 was considered significant.

Results

Respondents, 73 (51.8%) were female, 90 (63.8%) were single, 50 (35.5%) not more than 20 years of age, 76 (53.9%) attained secondary school as their highest educational status, 60 (42.6%) had monthly income of not more than NGN10000 while 89 (63.1%) were on Sodium

valproate (Table 1). The mean seizure control was approximately 2.21 ± 1.493 seizures in the past 4 weeks, that of quality of life was 2.43 ± 0.993 on the quality of Life in Epilepsy scale, medication adherence gave $5.89 \pm 2,551$ on the Modified Morisky Adherence Scale while the

number of medications was 1.98 ± 0.514 (Table 2).

Table 1: Socio-demographic of the respondents (N =141)

Variable	Number of respondents	Percentage (%)
Sex		
Female	73	51.8
Male	68	48.2
Marital status		
Married	34	24.1
Single	90	63.8
Widow/ separated	17	11.1
Age (Years)		
≤ 20	50	35.5
21-30	31	22.0
31-40	34	24.1
41-50	17	12.1
51-60	3	2.1
>60	6	4.2
Educational status		
No formal	5	3.6
Primary	32	22.7
Secondary	76	53.9
Tertiary	25	17.7
Average monthly income (Naira)		
≤ 10000	60	42.6
11000-20000	22	15.0
21000-30000	17	12.1
31000-40000	14	10.0
41000-50000	11	7.9
> 50000	17	12.1
Medication used		
Sodium valproate	89	63.1
Carbamazepine	72	51.1
Sodium valproate/ carbamazepine	15	10.6
Folic acid	107	75.9

Key: N = Sample size

Table 2: Descriptive statistics of variables

Variables	N	Mean	Std. Deviation
Seizure control	141	2.21	1.493
Quality of life	141	2.43	0.993
Medication adherence	141	5.89	2.551
Number of medications	141	1.98	0.514

Correlation analysis of P value for Seizure control and quality of life was <0.001, seizure control and medication adherence <0.001 while that of seizure control and number of medications taken by the patient was 0.017 (Table 3).

Table 3: Pearson correlations analysis of seizure control, quality of life, medication adherence and number of medications

Variables	Coefficient (R)	P values
Quality of life and Seizure control	-0.496	<0.001
Medication adherence and Seizure control	-0.471	<0.001
Number of medication and seizure control	0.088	0.017

The summary of multiple regression of quality of life, medication adherence, number of medication when seizure control was the dependent variable revealed that the coefficient (R) as 0.979, adjusted R^2 as 95.6% and standard error of estimate as 0.632 (Table 4). The Analysis of Variance "ANOVA" table provides an F test of 3,137 equal to 1072 where P<0.001 (Table 5). The detailed regression analysis of individual explanatory variables revealed that the standard coefficient of quality of life, medication adherence, number of medication(s) on epileptic seizure control were -0.076, 0.925, 0.176 respectively with their significant p values of <0.001, <0.001, <0.001 respectively (Table 6).

Table 4: Multiple regression analysis of quality of life, medication adherence, number of medication when seizure control

R	R^2	Adjusted R^2	Std. Error of the estimate	R^2 ▲	F ▲	Sig.
0.979[a]	0.959	0.958	0.632	0.959	1072	0.000

Key: ▲ = Change, St= Statistics, Std. = Standard, Sig= significant

Table 5: Analysis of variance of quality of life, medication adherence, number of medication and seizure control

Model	Sum of squares	Df	Mean square	F	Sig
Regression	1284.323	3	428.108	1072	<0.001
Residual	54.712	137	0.399		
Total	1339.035	140			

Table 6: Multiple Regressions model of Quality of life, Medication Adherence, Number of medication when Seizure control is dependent variable

Model	Unstandardized Co-efficients		Standardized co-efficients		Sig.	95% confidence interval	
	B	Std. error	Beta	T		Lower bound	Upper bound
(Constant)	2.134	0.323		6.614	<0.001	1.496	2.772
Quality of life	-0.024	0.006	-0.076	-3.850	<0.001	-.036	-.012
Medication adherence	1.121	0.024	0.925	47.173	<0.001	1.074	1.168
Number of medications	1.062	0.105	0.176	10.154	<0.001	.855	1.268

Sig = Significant, Std. Error = Standard Error

Discussion

This study found that about half of the respondents were female and about one-third of the respondents were married while slightly above half of the respondents were singles in their marital status. Similarity in the gender distribution observed in this study group had been seen elsewhere in United States of America [1] where they found out that slightly above half of the respondents were female. This was attributed to the fact that females are more given to attending hospitals and meeting up with their clinical checkups compared to their male counterparts [1].

About half of the respondents were in the age range of 18-30 years old while less than one-tenth were above 50 years of age. This confirmed previous study in southern Indian [8] where the majority of patients within the study population were within the range of 18-30 years of age, and also a study [10] in Shanghai, China posited that most patients with epilepsy fall between the ages of 10-30 years old. More also, about half of the respondents got secondary school education while about one-fourth attained tertiary level of education. Education among patients with epilepsy had also been an issue of concern. Findings from previous work have shown that epilepsy patients were less likely to continue higher education [9].

Sodium valproate was the commonly prescribed medication with nearly two-thirds of the respondents being placed on the

medication, followed by carbamazepine used by half of respondents, while about one-tenth of respondents were on both carbamazepine and sodium valproate. This was different from a study done in Taiwan [11] where phenytoin was the most frequently prescribed antiepileptic drug followed by valproic acid. In another research done in Indian [12], the most frequently prescribed antiepileptic drug was carbamazepine, then phenytoin and valproate. Almost three-quarter of the respondents in the study were on folic acid as an adjunct to antiepileptic medication. Folic acid helps to alleviate the teratogenicity of antiepileptic medications.

Quality of life in epilepsy, medication adherence and number of medications with seizure control showed a significant difference between group means as determined by one way ANOVA (F (3,137) =1072, p<0.001) in such a way that increase in the quality of life, medication adherence, and number of medications resulted in better seizure control in epilepsy. Similar study done in Malaysia [13] revealed that seizure control is related with medication adherence while research done [14] in Palestine refuted the claimed that seizure control has relationship with medication adherence.

In addition, quality of life in epilepsy, medication adherence and number of medication showed a significant relationship with seizure control following the result of multiple regression analysis which gave its coefficient as 0.979 indicating a strong

correlation between seizure control and the explanatory variables (quality of life in epilepsy, medication adherence and number of medication) and variability of seizure control as 95.6% for every additional increase in the explanatory variables.

For effect of individual variables, the relationship between seizure control and each of the explanatory variables revealed that seizure control is significantly related with quality of life as decrease in 0.076 of number of seizures lead to 1 unit increase in quality of life in epilepsy meaning improvements in one's quality of life brings about better seizure control. This finding of quality of life related with seizure control was corroborated by research [15] in Ethiopia. More also, seizure control was found to be significantly related with medication adherence in such a way that a 0.925 increase in the number of seizures will lead to an additional increase in the Modified Morisky Adherence Scale suggesting that increase medication adherence positively influence seizure control. Similar assertion [9] posited that patients of high adherence were those with higher quality of life. In the same way, the number of seizure episodes was found to be significantly related with the number of medications taken by the respondents as increase in 0.176 of number of seizure episodes will lead to an additional increase in the number of medications implying that increase in the number of medications taken by the patient for epilepsy leads to better seizure control.

Patients' medications adherence, quality of life and seizure control were assessed using self-reporting method of data collection, as this method has inherent limitations such as overestimation [16]. Future research is warranted to augment patient-reported data on adherence and seizure control with other measure of estimating such variables.

People who are suffering from epilepsy should be encouraged to adhere strictly to their medication regimen while caregivers, health professional and stakeholders of health should provide the needed conducive environment such as welfare scheme in order for the patient to afford the medication which will eventually improve the quality of life thus reducing seizure episodes in epilepsy [17].

Conclusion

Quality of life, medication adherence, and number of medications are correlated with seizure control. The combined effects of quality of life, medication adherence, and number of medications gave more than nine-tenth on variability of seizure control while their individual effects on the reduction of epileptic seizure episode are about one-tenth, nine-tenth, two-tenth respectively.

Acknowledgement

Conflict of Interest

No conflict of interest is associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. PTO designed the study, and managed the data, WJE wrote the manuscript. Both authors read and approved the final manuscript.

References

1. Hovinga CA, Asato MR, Manjunath R, Wheless JW, Phelps SJ, Sheth RD, Pina-Garza JE, Zingaro WM, Haskins LS. Association of non-adherence to antiepileptic drugs, seizures, quality of life, and productivity. Epilepsy Behav. 2008; 13: 316-322.
2. Birbeck GL, Hays RD, Cui X, Vickrey B. Seizure reduction and quality of life improvements in people with epilepsy. Epilepsia.2002; 43: 535-538

3. Hitiris N, Mohanraj R, Norrie J, Brodie MJ. Mortality in Epilepsy. Epilepsy Behavior. 2007; 10(3): 363-376.

4. Cramer JA, Scheyer RD, Mattson RH. Compliance declines between clinic visits. Arch Intern Med.1990; 150:1509-1510

5. Hayden M, Penna C, Buchanan N. Epilepsy: Patient perceptions of their condition. Seizure. 1992; 1:191-197.

6. Jones RM, Butler JA. Adherence to treatment in patients with epilepsy: associations with seizure control and illness beliefs. Seizure. 2006; 15 (7): 504-508

7. Fadare JO, Sunmonu TA, Bankole IA, Adekeye AA, Abubakar SA. Medication adherence and adverse effect profile of antiepileptic drugs in Nigerian patients with epilepsy. Neurodegenerative Disease Management. 2018; 8(1):25-36

8. Pourhoseingholi MA, Vahedi M, Rahimzadeh M. Sample size calculation in medical studies. Gastroenterological Hepatology from Bed to Bench.2013; 6(1):14-17

9. Nurulumi A, Nurul IO, Farida I. Medication adherence and quality of life in epilepsy patients. Int J Pharmacy and Pharmaceutical Sciences.2013; 5(2):401-403.

10. Huang M, Hong Z. The prevalence of epilepsy in rural Jinshan in Shanghai. Chinese J of Epid.2002; 23(5): 345- 346.

11. Juny S, Adepu R, Keshava BS. Assessment of antiepileptic drugs usage in a South Indian tertiary care teaching hospital. Neurology Asia.201318(2): 159 -165

12. Chen C, Yang L. Drug utilization pattern of antiepileptic drugs and traditional Chinese medicines in a general hospital in Taiwan - a pharmaco-epidemiologic study. J Clinical Pharmacy and Therapeutics.2000; 25 (2): 125-129.

13. Nagashekhara M, Kumar SG, Vasudra M, Lin L, Anil TM. Evaluation of self-reported medication adherence and its associated factors among epilepsy patients in Hospital. J Basic Clin Pharm.2016;7(4):105-109

14. Sweoleh WM, Ihbesheb M, Jara S, Taha ASA. Self-reported medication adherence and treatment satisfaction in patient with epilepsy. Epilepsy and Behaviour.2011;21(3):301-305.

15. Gebre AK, Amdemicheal S. Seizure control and quality of life in epilepsy in Makelle City, Northern Ethiopa. Behavioural Neurology, 2017; 28(6): 218-221.

16. Stephenson BJ, Rowe BH, Haynes RB, Macharia WM, Leon G. The rational clinical examination: is this patient taking the treatment as prescribed? JAMA; 1993.269:2779–2781

Niens LM, Van de Poel E, Cameron A, Ewen M, Laing R, Brouwer WBF. Practical measurement of affordability: an application to medicines. Bulletin of the World Health Organization. 2012; 90: 219-27