Journal of Pharmaceutical Research International

23(6): 1-11, 2018; Article no.JPRI.44377
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Pharmaceutical Care Intervention Improves Adherence to Antiepileptic Medication

Eshiet, Unyime Israel[1*], Okonta, J. Matthew[1] and Ukwe, Chinwe V.[1]

[1]Department of Clinical Pharmacy and Pharmacy Management, University of Nigeria, Nsukka, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Author EUI designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors OJM and UCV managed the analyses of the study. Authors OJM and UCV managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2018/44377
Editor(s):
(1) Dr. Mohamed Fathy, Professor, Faculty of Pharmacy, Assiut University, Assiut, Egypt.
Reviewers:
(1) Warren Boling, Loma Linda University, USA.
(2) Alarakol Simon Peter, Gulu University, Uganda.
Complete Peer review History: http://www.sciencedomain.org/review-history/26737

Original Research Article

Received 13 July 2018
Accepted 29 September 2018
Published 22 October 2018

ABSTRACT

Purpose: Adherence to the chronic pharmacotherapeutic regimen is poor resulting in negative therapeutic outcomes. Health education has been shown to improve the adherence of patients to their antiepileptic medication. The Pharmacist has the responsibility of providing patient education and counselling in the context of pharmaceutical care. The study aims to evaluate the efficacy of pharmaceutical care intervention on patients' adherence to prescribed self-administered antiepileptic medications.

Method: An opened, randomised, controlled, longitudinal and two-arm parallel prospective study with a 6-month patient follow up period was carried out on patients with epilepsy recruited from the medical and neurology out-patient clinics of two tertiary hospitals. Patients in the intervention group were provided with pharmaceutical care services. The impact of the pharmaceutical care intervention was evaluated by using the eight-Item Morisky Medication Adherence Scale. Repeated measure ANOVA was used to test the difference in the mean adherence score of the control and intervention groups over the time of intervention. The Pillai's Trace F was the corrected statistical test of choice for the model estimate, while the estimated effect was assessed with Partial etha.

**Corresponding author: E-mail: unyimeeshiet@uniuyo.edu.ng;*

Results: There was a statistically significant difference in medication adherence scores between the control and intervention group over time with F (2, 154) = 62.621, p= 0.000, partial η^2 = 0.45, as the mean medication adherence score of the intervention group increased from 3.70 (±1.60) at baseline to 4.04 (±1.42) and 6.89 (±0.77) at 3 months and 6 months respectively, indicating a substantial increase in medication adherence among patients in the intervention group compared with the control group where mean medication adherence scores were 3.86 (±1.69), 4.02 (±1.37) and 4.84 (±0.92) at baseline, 3 months and 6 months respectively.
Conclusion: Pharmaceutical care services implemented by a clinical pharmacist significantly improved the adherence to antiepileptic drugs in patients with epilepsy.

Keywords: Medication adherence; pharmaceutical care; antiepileptic drugs.

1. INTRODUCTION

A 2014 International League Against Epilepsy (ILAE) report defines epilepsy as a disease of the brain characterised by the following; at least two unprovoked or reflex seizures occurring greater than 24 hours apart, one unprovoked or reflex seizure with a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures occurring over the next 10 years, and a diagnosis of an epilepsy syndrome. Unprovoked in this context refers to the absence of a temporary or reversible factor that can lower the seizure threshold and induce a seizure [1].

There are a number of causes of increased mortality associated with epilepsy. Sudden unexplained death in epilepsy (SUDEP) has received a great deal of attention, as its manifestation is unanticipated and highly traumatic to the families of victims [2]. Postmortem studies have also reported the sub-therapeutic levels of antiepileptic drugs in some cases of SUDEP, indicating a poor adherence to AED treatment. Poor adherence to antiepileptic drug regimen appears to increase the risk of patients to SUDEP [3].

A study in the USA reported an association between poor adherence and increased mortality [4]. Hence, patients should be strongly encouraged to adhere to the prescribed antiepileptic drug regimen and to report any untoward effects that might affect adherence to their medication. This will help to reduce the risk of increased morbidity and mortality.

The goal of the treatment of epilepsy is to maintain a normal lifestyle by complete seizure control with minimal side effects. Treatment is divided into pharmacological and non-pharmacological methods. Antiepileptic drug therapy is the mainstay of treatment for majority of the patients. Non-pharmacological strategies are primarily reserved for drug-resistant epilepsy [5]. Antiepileptic drugs are medicines that prevent seizures in epileptic patients with side effects that are generally tolerable without adversely affecting the patients' quality of life. These drugs act on different molecular targets to alter the abnormal excitability of neurons selectively. This is achieved by preventing the spread of excitation or reducing the discharges of the focal seizure. Several antiepileptic drugs are available for the treatment of epilepsy [6].

Adherence, as defined by the World Health Organization (WHO) is the extent to which the persons' behaviour (including medication-taking) corresponds with agreed recommendations from a health care provider" [7]. It includes the commencement of the treatment, implementation of the prescribed therapeutic regimen, and discontinuation of the pharmacotherapy [8]. Often the term "compliance" is used in place of adherence, and the two can be used interchangeably in research and clinical practice. It describes the extent to which the patients' behaviour (including medication-taking) conforms to medical advice. However, its meaning has become more negative regarding patients' behaviour, since it implies patients' passivity [9]. Hence, the term "adherence" appears to be more commonly used in research and clinical practice.

Medication adherence is an important part of patient care and is indispensable in the attainment of clinical goals. Increasing the effectiveness of adherence to clinical interventions may elicit a greater impact on the health of the population than any improvement in specific medical treatment [7]. Medication non-adherence results in poor clinical outcomes increase in morbidity and mortality, and an increase in health care expenditure. Reports indicate that about 50%–60% of patients are non-adherent to the medicine prescribed by their

physician, particularly patients with chronic diseases. Greater than 30% of medication-related hospital admissions occur due to non-adherence medication [9].

Health education has been shown to improve the adherence of patients to their anti-epileptic medication [10]. It has been observed that patients' knowledge and understanding for their condition has a significant role to play in providing good quality outcomes for the patients. Pharmacists can contribute to positive therapeutic outcomes by educating the patient to empower them to follow their pharmacotherapeutic regimens. The Pharmacist has the responsibility of providing patient education and counselling in the context of pharmaceutical care. Pharmacists should encourage patients to seek education and should eliminate barriers to providing it [11,12]. A review by Reis et al. [13] only reported a little scientific evidence on the availability of pharmacist services to people with epilepsy. Therefore, the study aims to evaluate the efficacy of pharmaceutical care services in improving patients' adherence to prescribed self-administered antiepileptic medications.

2. MATERIALS AND METHODS

2.1 Study Design

This study was an opened, randomised, controlled, longitudinal and two-arm parallel prospective study with a 6-month patient follow up period.

2.2 Study Site

The study was conducted in the University of Uyo Teaching Hospital, Uyo, Akwa Ibom State and University of Calabar Teaching Hospital, Calabar, Cross River State. Both hospitals have tertiary health care facilities, serving as major referral centres with medical residents. The facilities run consultative outpatient clinics weekly in several specialities and sub-specialities.

2.3 Inclusion Criteria and Sampling Procedure

Patients were recruited from the neurology and medical out-patient clinics of the hospitals. The inclusion criteria were:

i. Patients diagnosed with epilepsy.
ii. Patients receiving treatment for epilepsy in the study sites.
iii. Patients who provided written informed consent to participate in the study.

The exclusion criteria were:

i. Patients who were diagnosed with having non-epileptic seizures only.
ii. Patients who were less than 16 years.
iii. Patients who expressed willingness to withdraw from the study.
iv. Mentally retarded patients.
v. Patients with acute psychiatric illness.

The study was conducted during May 2016 to March 2018. All the patients presented at the study centres within the period of study and met the inclusion criteria were recruited. The case notes of the selected participants were assigned numbers which represented individual patients. The patients were then randomly assigned to one of the two groups (intervention or control group) based on the number on their case notes using an online randomisation software [http://www.randomization.com]. Patients in the control group received the usual care provided in the study sites while patients in the intervention group were provided with pharmaceutical care services in addition to the usual care.

2.4 Intervention

Pharmaceutical care services were provided to the patients in the intervention group. The Pharmaceutical care intervention consisted of an educational treatment programme implemented by a clinical pharmacist. This programme was adapted with modifications from a previous educational programme developed for patients with epilepsy and their relatives (MOSES) [14]. The teaching program focused on improving patients' knowledge regarding epilepsy and its therapeutic management amongst other relevant topics. Specific emphasis was placed on adherence to antiepileptic therapy during the programme. The medical and educational contents of the teaching programme were evaluated by a neurologist before administration to the patients. The teaching program was implemented by a research clinical pharmacist with the aid of research assistants who were nurses working at the neurology unit of the hospital. The teaching programme within the context of pharmaceutical care was delivered to the patients during their clinic appointments and reinforced on follow up meetings fortnightly. The strategy of addressing underlying reasons for medication non-adherence, counselling patients,

and providing serial follow-up through reminder calls and text messages was implemented.

2.5 Data collection Instrument/Evaluation of Impact of Intervention

The impact of the pharmaceutical care intervention on the adherence of patients to prescribed self-administered anti-epileptic drugs was determined by using the English version of the eight-Item Morisky Medication Adherence Scale (MMAS-8).

Assessing adherence is of immense importance to both researchers and clinicians. Medication adherence measures should be low cost and user friendly, easy to carry out, highly reliable, flexible and practical. Unfortunately, there is no single measure that can meet all these gold standards as each tool has its own disadvantages. Questionnaires and scales have been designed to standardise the measurement of adherence to a specific medication regimen with the aim of minimising the limitations of other self-report methods. These questionnaires are usually validated against both subjective and objective measures [15]. There are many questionnaires and scales for the assessment of medication adherence, however, only a few are considered as being very useful in covering the concept of medication-taking behaviours, barriers to adherence, and the belief associated with adherence [9,16,17,18]. Self-report questionnaires are preferred in a busy, resource-limited clinical setting with a moderate to high literacy population [9]. The low cost, simplicity, and real-time feedback provided by self-report questionnaires such as the eight-item Morisky medication adherence scale (MMAS-8) developed by Morisky et al. [18] have contributed to their popularity and continuous use in clinical practice.

MMAS-8 is an adherence scale with proven validity and reliability in patients with chronic diseases. As a result, it is probably the most accepted self-report measure for adherence to medication [18]. In the MMAS-8, a higher score indicates a higher adherence level. Scores less than 6 shows low adherence, scores between 6 and less than 8 indicates medium adherence, while the maximum score of 8 shows high adherence to medication.

2.6 Data Collection

Study participants were interviewed with the MMAS-8 in thrice during the course of the study. The first time (T_1) was immediately before implementation of the pharmaceutical care intervention, and the second (T_2) and third time (T_3) were after three and six months of implementation of the intervention respectively. Each participant was interviewed individually during his/her clinic appointments at the appropriate, predetermined time intervals (i.e. at T_1, T_2 and T_3 respectively). The participants were neither coerced nor induced or compensated for participating in the study.

2.7 Statistical Analysis of Data

Frequencies and proportions were used to present the data at the univariate level. The student t-test was used to evaluate the difference in socio-demographic characteristics between patients in control and the intervention groups. To evaluate the impact of the intervention, the repeated measure ANOVA was used to test the difference in the mean adherence score of the control and intervention groups over the time of intervention. The Pillai's Trace F was the corrected statistic test of choice for the model estimate, while the estimated effect was assessed with Partial etha; the closer the value of Partial etha is to 1, the stronger the effect. ANOVA analysis was conducted after checking that all data met the criteria and assumptions for carrying out repeated ANOVA.

A difference-in-difference analysis was also employed to evaluate the outcome of the intervention. Difference-in-difference analysis subtracts the difference between the baseline and end line in the control group from the difference between baseline and end line in the intervention group. This approach removes the counterfactual, i.e. what would have happened even if there was no intervention. The extent of change is indicated by how positive or negative the values are.

Quantitative data were analysed using Statistical Program for the Social Sciences (SPSS) version 17.0 computer package with descriptive statistics. A prior level of significance ($p< 0.05$) was used for all comparisons.

2.8 Ethical Approval

The research protocol was approved by the Health Research Ethics Committees of the University of Uyo Teaching Hospital and University of Calabar Teaching Hospital (Reference numbers:

UUTH/AD/S/96/VOL.XIV/571 & UCTH/HREC/33/454). In addition, an informed consent was obtained from the participants before recruitment into the study.

3. RESULTS

A total of 157 patients (79 patients in the intervention group and 78 patients in the control group) completed the study. The patient flow is shown in Fig. 1.

The socio-demographic profile of the patients in the control and intervention groups is presented in Table 1.

3.1 Test of Difference in Mean Medication Adherence Scores of patients in Control and Intervention Groups at baseline (pre-intervention), Midline (3 months post-intervention) and End-line (6 months-intervention)

The overall mean medication adherence score of patients in the control group increased from 3.86 (±1.69) to 4.02 (±1.37) and 4.84 (±0.92) at 3 months and 6 months respectively, however, there was a more significant increase in the overall mean score for medication adherence among patients in the intervention group as the mean adherence score increased from 3.70 (±1.60) to 4.04 (±1.42) at 3 months and 6.89 (±0.77) at 6 months, indicating an increase in medication adherence among patients in the intervention group compared with the control group. There was a statistically significant difference in medication adherence scores between the control and intervention group over time with $F(2, 154) = 62.621$, $p=0.000$, partial $\eta^2 = 0.45$.

3.2 Difference-in-Difference Analysis at 3 Months and 6 Months Post-Intervention

The difference-in-difference analysis at 3 months post-intervention showed that the pharmaceutical care services provided by the clinical pharmacist resulted in an increase in the mean medication adherence score from the baseline value by 0.18 points. The difference-in-difference analysis at the end of the intervention showed that the implementation of pharmaceutical care services for 6 months resulted in an increase in the mean medication adherence score from the baseline value by 2.21 points.

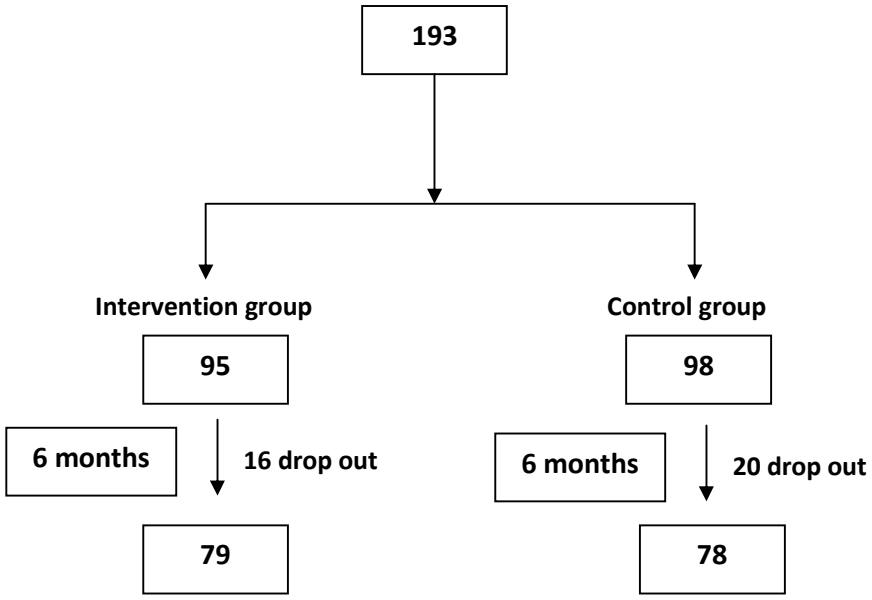

Fig. 1. Depiction of the study design with the number of patients randomised to each group and dropouts in each group.

Table 1. Socio-demographic characteristics of patients

	Control		Intervention		Student t-test	
	Frequency	Proportion (%)	Frequency	Proportion (%)	t	p value
Age group						
16-24	19	24.40	27	34.20	1.115	0.267
25-34	23	29.50	21	26.60		
35-44	9	11.50	12	15.20		
>=45	27	34.60	19	24.10		
Sex						
male	45	57.70	48	60.80	0.389	0.698
female	33	42.30	31	39.20		
Educational Level						
Primary	6	7.69	4	5.06	-o.433	0.666
Secondary	27	34.62	21	26.58		
Tertiary	45	57.69	54	68.35		
Marital status						
single	46	59.00	46	58.20	-0.058	0.954
married	29	37.20	30	38.00		
widowed	3	3.80	3	3.80		
Religion						
Christianity	76	97.40	78	98.70	0.591	0.555
Islam	2	2.60	1	1.30		
Employment status						
employed	29	37.20	24	30.40	-0.370	0.712
unemployed	29	37.20	37	46.80		
self employed	16	20.50	13	16.50		
retired	4	5.10	5	6.30		
Monthly income (NGN)*						
no income	29	37.20	36	45.60	0.956	0.341
<30,000	9	11.50	9	11.40		
30,000 - 50,000	9	11.50	5	6.30		
51,000 - 70,000	5	6.40	9	11.40		
71,000 - 100,000	16	20.50	11	13.90		
>100,000	10	12.80	9	11.40		

**NGN = Nigerian Naira*

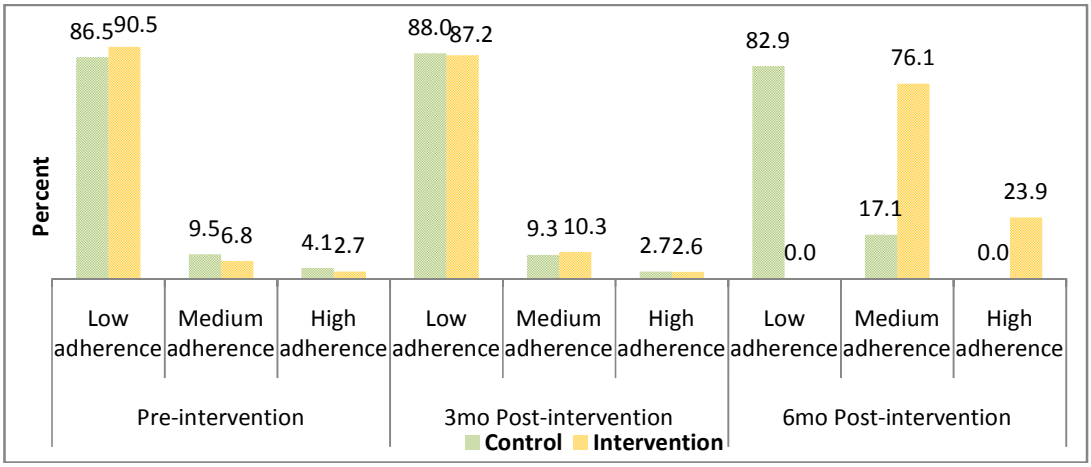

Fig. 2. Effect of Pharmaceutical Care Services on Patients' Adherence to Antiepileptic medication (Using the Eight-Item Morisky Medication Adherence scale)

Table 2. Clinical characteristics of patients

Characteristics	Control		Intervention		Student's t-test	
	Frequency	%	Frequency	%	t	P
Duration of epilepsy						
≤2 years	20	25.6	22	27.8	-1.662	0.099
3-5 years	19	24.4	13	16.5		
≥6 years	39	50.0	44	55.7		
Presence of co-morbidity						
None	51	65.4	60	75.9	-1.606	0.110
Yes	27	34.6	19	24.1		
Type of co-morbidity*						
	Control		**Intervention**		**Total**	
Hypertension	16 (59.3%)		8 (42.1%)		24 (52.2%)	
HIV	1 (3.7%)		2 (10.5%)		3 (6.5%)	
Peptic ulcer disease	3 (11.1%)		0		3 (6.5%)	
Hypertension + Benign Prostatic hyperplasia	3 (11.1%)		4 (21.1%)		7 (15.2%)	
Tuberculosis	2 (7.4%)		0		2 (4.3%)	
Hypertension + diabetes mellitus	1 (3.7%)		1 (5.3%)		2 (4.3%)	
Hypertension + asthma	1 (3.7%)		1 (5.3%)		2 (4.3%)	
Leukaemia	0		1 (5.3%)		1 (2.2%)	
Hepatitis	0		2 (10.5%)		2 (4.3%)	

**Among patients who presented with Co-morbidity*

Table 3. Mean scores of patients' medication adherence and test of difference over Time

Medication adherence score	Group	Mean	Std. Deviation	95% Confidence Interval	
				Lower Bound	Upper Bound
Pre-intervention	Control	3.86	1.69	3.4	4.2
	Intervention	3.70	1.60	3.3	4.0
3 months Post-intervention	Control	4.02	1.37	3.7	4.3
	Intervention	4.04	1.42	3.7	4.3
6 Months Post-intervention	Control	4.84	0.92	4.6	5.0
	Intervention	6.89	0.77	6.7	7.0
Test statistic	Pillai's Trace F (2, 154) = 62.621 p = 0.000 Partial η2 = 0.45				

Table 4. Difference-in-difference analysis evaluation at 3 months post-intervention

Group	Baseline adherence score	3 Months adherence score	Difference	Difference – in- Difference	Remarks
Control	3.86	4.02	0.16		Increased
Intervention	3.70	4.04	0.34	0.18	adherence

Table 5. Difference-in-difference analysis evaluation at 6 months post-intervention

Group	Baseline adherence score	6 Months adherence score	Difference	Difference – in-Difference	Remarks
Control	3.86	4.84	0.98		Increased
Intervention	3.70	6.89	3.19	2.21	adherence

4. DISCUSSION

Medication non-adherence to pharmacotherapy, especially among patients with chronic conditions is a prevalent and expensive problem. The mean medication adherence score of the patients in this study at baseline (pre-intervention) indicated a low level of adherence. A remarkably significant increase in medication adherence over time among patients that participated in the educational programme implemented by the pharmacist when compared with the patients who did not participate in this programme was recorded. Also, the partial etha value of 0.45 as highlighted in this study indicates a substantial effect of the pharmaceutical care intervention on the patients' adherence to prescribed antiepileptic drugs. Furthermore, the result of the difference-in-difference analysis clearly showed that the pharmaceutical care intervention significantly increased adherence to antiepileptic medication. Unfortunately, in this study, a poor involvement of pharmacist in the management of epilepsy was also recorded.

In this study, the low level of medication adherence at baseline is consistent with findings from other studies [19-22]. Medication non-adherence is particularly problematic for asymptomatic conditions, such as epilepsy, hypertension and hyperlipidemia, despite a favourable tolerability profile of many medications used in their treatment [19].

The success of the pharmaceutical care intervention employed in this study might be due to the strategy of addressing underlying reasons for medication non-adherence, counselling patients, and providing serial follow-up. This strategy conformed to the recommendations of other researchers and employed in the Federal Study of Adherence to Medications in the Elderly (FAME). FAME was a multiphase, single-centre study of the efficacy of a comprehensive pharmacy care program, which included patient education and an adherence aid (medications custom packaged in blister packs) to improve medication adherence among military health care beneficiaries aged 65 years, or older who were prescribed at least 4 chronic medications per day [19,23]. A study on 152 people with epilepsy by Dash et al. [24] endorsed that a structured educational treatment program was effective in increasing scores in the MMAS. In this study, the mean scores in the MMAS of the epilepsy health education group were 6.18 and 7.53 before and after health education respectively, thus proving the efficacy of an educational treatment program in improving drug adherence in people with epilepsy [24].

The research findings point to the fact that pharmacists are essential health care professionals that can provide effective counselling and education services to patients with epilepsy. It also underscores the need for pharmacists to actively participate in the management of epilepsy. Furthermore, it reveals gaps in the management of epilepsy that can be filled by pharmacists.

A study in Malaysia found almost 60% of the study population defaulting in their antiepileptic drug doses prior to seizure attacks. In this report, non-adherence to antiepileptic drug regimen accounted for about 65% of the drug therapy problem identified and was also a major factor for uncontrolled epilepsy [25]. By providing pharmaceutical care services to people with epilepsy, pharmacists can optimise antiepileptic drug therapy and help to achieve desired treatment goals.

The observation of a poor involvement of pharmacist in the management of epilepsy might be an indication of a lack of interest of pharmacists in providing specialised care to people living with epilepsy. Pharmacists are important health professionals in counselling and monitoring patients with epilepsy because they are easily accessible and have sufficient knowledge of pharmacotherapy, health education, and management of chronic diseases [26]. However, Reis et al. [13] reported that little evidence is available in the scientific literature regarding the pharmacists' services to patients with epilepsy [13]. Although the number of articles highlighting pharmacists' involvement in epilepsy is low, results from these studies revealed the positive impact of the pharmacists' contribution. In these studies, the pharmacists' interventions were essential to improving the health of the people with epilepsy they served. The reports indicated that pharmacists' interventions were able to prevent drug therapy problems. Pharmacists contributions also led to improved the medication adherence and response to pharmacotherapy [13]. All of these studies reported significant achievements and confirmed that including pharmacists in the therapeutic team produces effective results for the success of pharmacotherapy and the quality of life of people with epilepsy. Unfortunately, it is difficult to find pharmacists to work with

pharmacist-led epilepsy consultations [27]. Although, there are practical limitations to the wide-scale implementation of a comprehensive pharmacist led interventional programs, these limitations must be recognised and overcome to ensure its effectiveness for improving medication adherence. For instance, in several countries, clinical services provided by pharmacists are not reimbursed. This discourages the pharmacists from providing these services [28, 29]. Moreover, lack of information and understanding among physicians, other health professionals, and patients about how pharmacists can contribute to seizure control and quality of life of people with epilepsy can also hamper the deployment and implementation of pharmaceutical care services. In contrast, the poor involvement of pharmacists in the care of patients with epilepsy might be a reflection of pharmacists' knowledge gaps in the holistic management of epilepsy, a factor that may inhibit them from performing such clinical services. For this narrative to change, pharmacists must be trained on epilepsy, pharmacotherapy, and the skills needed to provide counselling and education to patients [30].

Given the pervasive and morbid effects of medication non-adherence, pharmacists should lay great emphasis not only the provision of antiepileptic medications, but also on adherence to prescribed antiepileptic drugs.

5. CONCLUSION

Pharmaceutical care services included an educational treatment programme implemented by a clinical pharmacist substantially improved adherence to antiepileptic drugs in patients with epilepsy. This reveals the positive impact of pharmacists' involvement in the management of people living with epilepsy.

6. STUDY STRENGTH

The principal strength of the study is in its design, being a randomised, controlled, longitudinal and two-arm parallel prospective study with patients in both groups having comparable socio-demographic and clinical characteristics.

7. STUDY LIMITATION

The use of a subjective method of assessing medication adherence may be viewed as a limitation of the study.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross H, Elger CE, Engel J Jr, Forsgren L, French JA, Glynn M, Hesdorffer DC, Lee BI, Mathern GW, Mosh SL, Perucca E, Scheffer IE, Tomson T, Watanabe M, and Wiebe S. A practical clinical definition of epilepsy. Epilepsia. 2014;55(4):475–482.
2. Thurman DJ, Hesdorffer DC, and French JA. Sudden unexpected death in epilepsy: Assessing the public health burden. Epilepsia. 2014;55(10):1479–1485.
3. Scottish Intercollegiate Guidelines Network (SIGN). Diagnosis and management of epilepsy in adults. Edinburgh: SIGN; 2015. (SIGN publication no. 143; May 2015).
4. Faught E, Duh MS, Weiner JR, Guerin A, Cunnington MC. Nonadherence to antiepileptic drugs and increased mortality Findings from the RANSOM Study. Neurology 2008;71(20):1572-8.
5. Nwani PO, Asomugha LA, Arinze EO, Ewereji KO, Nwosu MC, Oguniyi A. Patterns of antiepileptic drugs use and seizure control among people with epilepsy in a surburban community in southeast Nigeria. African Journal of Neurology 2012;31(2):36-42.
6. Redd DS. Clinical pharmacology of current antiepileptic drugs. Int J Pharm Sci Nanotech. 2014;7(1).
7. Sabate E. Adherence to long-term therapies: Evidence for action. World Health Organization, Geneva, Switzerland; 2003.

8. Vrijens B, de Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppar T, Dobbels F, Fargher E, Morrison V, Lewek P, Matyjaszczyk M, Mshelia C, Clyne W, Aronson JK, Urquhart J. A new taxonomyfor describing and defining adherence to medications. British Journal of Clinical Pharmacology. 2012;73(5): 691–705.
9. Lam WY, Fresco P. Medication adherence measures: An overview. BioMed Research International Volume 2015, Article ID 217047, 12 pages. Hindawi Publishing Corporation.
10. Ibinda F, Mbuba CK, Kariuki SM, Chengo E, Ngugi AK, Odhiambo R, Lowe B, Fegan G, Carter JA, Newton CR. Evaluation of Kilifi epilepsy education programme: A randomized controlled trial. Epilepsia. 2014;55(2):344–352.
11. American Society of Health-System Pharmacists. ASHP guidelines on a standardized method for pharmaceutical care. Am J Health-Syst Pharm. 1996;53:1713–6.
12. Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. American Journal of Health Systems Pharmacy. 1990;47:533-543.
13. Reis TM, Campos MS, Nagai MM, Pereira LR. Contributions of pharmacists in the treatment of epilepsy: A systematic review. Am J Pharm Benefits, 8(3):e55-e60.review. British Journal of Clinical Pharmacology. 2016;77(3):427–445.
14. Ried S, Specht U, Thorbecke R, Goecke K, Wohlfa R. MOSES: An educational program for patients with epilepsy and their relatives. Epilepsia. 2001;42(Suppl. 3):76–80. Blackwell Science, Inc.
15. Tan X, Patel I, Chang J. Review of the four item Morisky medication adherence scale (MMAS-4) and eight item Morisky Medication Adherence Scale (MMAS-8). Innovationsin Pharmacy. 2014;5(3): 165.
16. Lavsa SM, Holzworth A, Ansani NT. Selection of a validated scale for measuring medication adherence. J Am Pharm Assoc. 2011;51(1):90-94.
17. Krousel-Wood M, Joyce C, Holt EW, Levitvan EB, Dornelles A, Webber LS, Munter P. Development and evaluation of a self-report tool to predict low pharmacy refill adherence in elderly patients with uncontrolled hypertension. Pharmaco-therapy. 2013;33(8):798–811.
18. Morisky DE, Ang A, Krousel-Wood M, and Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. Journal of Clinical Hypertension. 2008;10(5):348–354.
19. Jeannie KL, Karen AG, Allen JT. Effect of a pharmacy care program on medication adherence and persistence, blood pressure and low-density lipoprotein cholesterol. A randomized controlled trial. JAMA. 2006;296(21):2563-2571.
20. Blackburn DF, Dobson RT, Blackburn JL, Wilson TW. Cardiovascular morbidity associated with nonadherenceto statin therapy. Pharmacotherapy. 2005;25:1035-1043.
21. Abughosh SM, Kogut SJ, Andrade SE, Larrat P, Gurwitz JH. Persistence with lipid-lowering therapy: Influence of the type of lipid-lowering agent and drug benefit plan option in elderly patients. J Manag Care Pharm. 2004;10:404-411.
22. Jackevicius CA, Mamdani M, Tu JV. Adherence with statin therapy in elderly patients with and without acute coronary syndromes. JAMA. 2002;288:462-467.
23. Becker MH, Maiman LA. Strategies for enhancing patient compliance. J Community Health. 1980;6:113-135.
24. Dash D, Sebastian TM, Aggarwal M, Tripathi M. Impact of health education on drug adherence and self-care in people with epilepsy with low education. Epilepsy & Behavior. 2015;44:213–217.
25. Manan MM, Rusli RA, Ang WC, Al-Worafi YMA, Ming LC. Assessing the pharmaceutical care issues of antiepileptic drug therapy in hospitalised epileptic patients. Journal of Pharmacy Practice and Research. 2014;44(3):83-88.
26. Ratanajamit C, Kaewpibal P, Setthawacharavanich S, Faroongsarng D. Effect of pharmacist participation in the health care team on therapeutic drug monitoring utilization for antiepileptic drugs. J Med Assoc Thai. 2009;92(11): 1500-1507.
27. Fogg A, Staufenberg EF, Small I, Bhattacharya D. An exploratory study of primary care pharmacist-led epilepsy consultations. Int J Pharm Pract. 2012;20(5):294-302.

28. Berdine HJ, Skomo ML. Development and integration of pharmacist clinical services into the patient-centered medical home. J Am Pharm Assoc. 2012;52(5):661-667.
29. MacLaren R, Brett MR, Campbell J. Clinical and financial impact of pharmacy services in the intensive care unit: pharmacist and prescriber perceptions. Pharmacotherapy. 2013;33(4):401-410.
30. Alaqeel A, Alebdi F, Sabbagh AJ. Epilepsy: What do health-care professionals in Riyadh know? Epilepsy Behav. 2013;29(1):234-237.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history/26737