

# Identification and Resolution of Drug-related Problems Encountered by Individuals with Epilepsy in Nigeria

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## Abstract

**Objective:** Interventions by clinical pharmacists are required to identify and resolve medication-related problems. This study aimed to identify drug-related problems (DRPs) encountered by patients with epilepsy, provide pharmaceutical care (PC) interventions, and evaluate the impact of these clinical interventions.

**Methods:** A prospective longitudinal study was conducted on 95 patients with epilepsy attending the neurology/medical outpatient clinics of two epilepsy referral centers. During patient clinic visits, the pharmacist collected medication history, reviewed patient medication use, identified DRPs, provided PC services, and collaborated with physicians and patients to resolve identified DRPs. Documentation and classification of identified DRPs, categorization of the pharmacists' interventions, categorization of acceptance of the pharmacist's intervention proposals, and categorization of the status of the DRPs after the interventions were performed using the Pharmaceutical Care Network Europe Classification Scheme for DRPs V8.02.

**Results:** The total number of DRPs identified by the clinical pharmacists in the study population was 277. Three hundred and seventy-nine interventions were offered by the clinical pharmacists. Approximately 57.04% of the identified DRPs were patient-related, whereas 15.88% were dispensing-related. Approximately 64.12% of the research pharmacist's interventions were at the patient level, whereas 24.01% of these interventions were at the prescriber level. Two hundred and eleven (55.67%) of the clinical pharmacist interventions were accepted and fully implemented. Approximately 61.73% of the identified DRPs were fully resolved.

**Conclusion:** Most DRPs encountered were resolved following the acceptance of the clinical pharmacist's PC interventions by the patients and attending physicians. This study revealed the huge potential of clinical pharmacists in providing specialized care for patients with epilepsy.

**Keywords:** Pharmaceutical care, epilepsy, drug-related problems

## INTRODUCTION

An estimated 70 million people are reportedly living with epilepsy globally, with approximately 95% of this population living in developing parts of the world. The disease is ranked as the second most frequently encountered neurological condition, with a worldwide prevalence of 5-9 persons per 1,000 population.<sup>1,2</sup>

Anti-seizure medication is the first line of treatment for most epileptic patients with the goal of sustaining a normal lifestyle through absolute seizure control with minimal or no side effects.<sup>3</sup>

The role of pharmacists has evolved over the years to involve a variety of responsibilities, from dispensing medications to patient care, patient counselor, health care educator, and community service to clinical practice. Recommendations by the Joint Commission on Accreditation of Healthcare Organizations state that all prescriptions must be evaluated by pharmacists before dispensing and emphasize that outcomes should be documented as a result of direct patient care by the pharmacist.<sup>4</sup>

In 1990, Hepler and Strand<sup>5</sup> defined pharmaceutical care (PC) as "the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life". Medication errors are errors encountered during ordering, transcribing, dispensing, administering, and monitoring in the process of medication use. Interventions by pharmacists are required to identify and

resolve drug-related problems (DRPs). Many of these problems can be prevented by educating healthcare providers about them. These clinical interventions by pharmacists have a positive impact on the healthcare system by enhancing patient care and reducing costs. It is important to ensure that all interventions by the pharmacist are documented. This will help justify pharmacists' services to patients, healthcare administrators and providers, and patient care takers. It also helps to strengthen the profession and its image in the society.<sup>4,6</sup>

PC is ideally provided by a clinical pharmacist who is part of a multidisciplinary team that provides care to the patient. Medication reviews are a part of PC interventions to reduce inappropriate prescribing and drug use. This is the process in which a pharmacist reviews the patient, their disease, and drug treatment. PC enables pharmacists to implement interventions designed to reduce inappropriate prescribing and drug use. It also helps identify unmet therapeutic needs.<sup>7</sup>

Reports from previous studies have shown that pharmacists' interventions were essential to improving the health of patients with epilepsy. These reports indicate that pharmacists' interventions can prevent drug therapy problems. However, more studies are needed to highlight the positive impacts of pharmaceutical services on the health of patients with epilepsy.<sup>8</sup>

In Nigeria, evidence of the involvement of pharmacists in the provision of specialized care to patients with epilepsy is lacking. This study aimed to identify DRPs encountered by patients with epilepsy using PC instruments; provide PC interventions to resolve identified DRPs; and determine the status of the DRPs after the implementation of PC interventions.

## METHODS

### Study Design and Setting

This was a prospective longitudinal study with a 6-month follow up period.

The study sites were the University of Uyo Teaching Hospital in Uyo, Akwa Ibom State, and the University of Calabar Teaching Hospital in Calabar, Cross River State. These selected hospitals are major referral centers for epilepsy management in Southern Nigeria. Patients were recruited from the neurology and medical outpatient clinics of the hospitals.

### Study Population

Ninety-five patients diagnosed with epilepsy and receiving treatment for epilepsy at selected hospitals who fulfilled the

inclusion criteria were identified and recruited into the study. The Inclusion criteria were patients diagnosed with epilepsy and receiving treatment for epilepsy at the study sites, those who provided written informed consent to participate in the study, and those who expressed willingness to abide by the rules of the study.

The exclusion criteria were patients who were diagnosed with non-epileptic seizures only, those aged less than 16 years, those who expressed willingness to withdraw from the study, those with intellectual disabilities, and those with acute psychiatric illness.

### Pharmaceutical Services

In this study, PC intervention was aimed at identifying and resolving DRPs encountered by patients. The research clinical pharmacist interacted with the physicians and patients during each clinic visit to optimize therapy with anti-seizure medications. PC was provided in a stepwise approach:

Setting priorities for patient care;

Assessing patients' specific educational needs and identifying DRPs;

Developing a comprehensive and achievable PC plan in collaboration with the patient and physician;

Implementation of this plan;

Monitoring and review of the plan from time to time according to the needs of the patient.

During each clinic visit, patients met with the research pharmacist prior to visiting their physician. The research pharmacist collected medication history, identified DRPs, collaborated with the physician and patients to resolve identified problems, answered questions on drug therapy, and encouraged adherence.

The research pharmacist also provided counseling services to the patients during their clinic visits. When necessary, the pharmacist provided relevant recommendations for consideration by the physician when making an overall treatment plan. Patients were also provided with a report diary with the time and date of an appointment following each visit. The patient report diary contains a table for the patients to record the time that they took their anti-seizure drugs and the time that they had a seizure or experienced unusual symptoms. The patients were also requested to document in the diary the name and dose of the anti-seizure medication taken, the frequency of administration, the time each dose was taken, the side effects experienced (if any), and the anti-seizure medication suspected.

### Assessment of Pharmaceutical Intervention

The type and incidence of DRPs, as well as the type of intervention provided, the acceptance or rejection of the intervention, and whether the problem was resolved or not were documented using the Pharmaceutical Care Network Europe (PCNE) Classification Scheme for Drug-related Problems version 8.02.

The PCNE classification is used for research into the nature, prevalence, and incidence of DRPs. Moreover, it is used as a process indicator in experimental studies on PC outcomes. This

#### MAIN POINTS

- Involvement of pharmacists in the provision of specialized care to patients with epilepsy are lacking in Nigeria.
- Pharmaceutical care (PC) enables pharmacists to implement interventions to reduce inappropriate drug use.
- This study revealed the great potential of pharmacists in providing specialized care for persons with epilepsy.
- Providing justification for the integration of PC services with other elements of health care for patients with epilepsy.

tool is intended to help healthcare professionals document DRP information during the PC process.

The following official definition of PCNE-DRP is the basis for the classification:

*“A Drug-Related Problem is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes”.*<sup>9</sup>

The basic PCNE classification now has 3 primary domains for problems, 8 primary domains for causes and 5 primary domains for Interventions. A section called ‘Acceptance of the Intervention Proposals’ is added, including 3 domains. However, on a more detailed level there are 7 grouped sub-domains for problems, 35 grouped sub-domains for causes, 16 grouped sub-domains for interventions, and 10 sub-domains for intervention acceptance. These sub-domains can be considered an explanation of the principal domains. A scale is also added to indicate whether or to what extent the problem has been solved, containing 4 primary domains and 7 sub-domains.<sup>9</sup>

**Statistical Analysis**

Data were analyzed using IBM Statistical Products and Services Solutions (SPSS) for Windows, version 25.0 (IBM Corp, version 25.0 Armonk, NY, USA). Frequencies and proportions were used to summarize the data. The analyzed data were presented using the PCNE classification scheme for DRPs version 8.02.

**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. Dates: 25: 04: 2016 & 11: 04: 2016 respectively). In addition, informed consent was obtained from the participants prior to their recruitment into the study.

**RESULTS**

Ninety-five patients with epilepsy were recruited into the study. The sociodemographic and clinical profiles of the patients are presented in Table 1.

**Identification and Resolution of Drug-related Problems**

The classification and sub-classification of DRPs, categorization and sub-categorization of interventions by the research pharmacist, acceptance of the research pharmacist’s intervention proposals, and the categorization of the status of the DRPs after the intervention proposals are presented in Tables 2, 3, 4, and 5, respectively.

The total number of DRPs identified by the research pharmacist among patients with epilepsy was 277. Three hundred and seventy nine (379) interventions were offered by the research pharmacist.

Approximately 57.04% of the identified DRPs were patient-related, whereas 15.88% were dispensing-related. Approximately 64.12% of the research pharmacist’s interventions were at the patient level, whereas 24.01% of these interventions were at the prescriber level.

Approximately 61.73% of the identified DRPs were fully resolved after implementation of PC interventions.

**DISCUSSION**

PC involves identifying the medication needs of an individual patient and providing not only the required medicines but also the necessary clinical services before, during, or after treatment to ensure an optimally safe and effective drug therapy.<sup>10</sup> This describes the principal essence of clinical pharmacy, from where it was adopted as a professional practice rather than merely a health science, and provides a way for clinical pharmacists, particularly specialists and subspecialists, to coordinate their clinical work more effectively.<sup>11</sup>

Two hundred and seventy-seven DRPs were identified by the research pharmacist among the patients who participated in the study. Three hundred and seventy-nine intervention proposals were offered by the research pharmacist, while one hundred and sixty-one of the identified DRPs were fully resolved. Although interventions were made at both the prescriber and patient levels, most of the interventions in this study were at the patient level. This is because most of the identified DRPs were patient-related.

**Table 1.** Socio-demographic/clinical characteristics of patients

Characteristics	Frequency	Percentage
<b>Age (years)</b>		
16-24	29	30.53
25-34	25	26.32
35-44	19	20.0
≥45	22	23.16
<b>Sex</b>		
Male	54	56.84
Female	41	43.16
<b>Educational level</b>		
Primary	11	11.58
Secondary	31	32.63
Tertiary	53	55.79
<b>Marital status</b>		
Single	49	51.58
Married	38	40.0
Widowed	8	8.42
<b>Religion</b>		
Christianity	93	97.89
Islam	2	2.11
<b>Duration of illness</b>		
≤2 years	27	28.42
3-5 years	20	21.05
≥6 years	48	50.53
<b>The type of epilepsy</b>		
Generalized tonic clonic	64	67.37
Focal onset awareness	9	9.47
Impaired awareness	11	11.58
Diverse seizures	8	8.42
Absence seizures	3	3.16

Table 2. Classification and sub-classification of drug-related problems

Primary domain	Causes of DRPs	Total	Domain proportion	Overall proportion
<b>1. Drug selection</b>	Inappropriate drug according to guidelines/formulary	0	-	-
	Inappropriate drug (within the guidelines but not recommended) contra-indicated	0	-	-
	No indication for drug	0	-	-
	Inappropriate combination of drugs or herbal products medication	13	39.39	4.69
	Inappropriate duplication of therapeutic or active groups ingredient	9	27.27	3.24
	No drug treatment in spite of existing indication	11	33.33	3.97
	Too many drugs prescribed for indication	0	-	-
	<b>Sub-total</b>	<b>33</b>	<b>-</b>	<b>11.91</b>
<b>2. Drug form</b>	Inappropriate drug form	0	-	-
	<b>Sub-total</b>	<b>0</b>	<b>-</b>	<b>-</b>
<b>3. Dose selection</b>	Drug dose too low	0	-	-
	Drug dose too high	0	-	-
	Dosage regimen not frequent enough	0	-	-
	Too frequent dosage regimen	0	-	-
	Dose timing instructions are incorrect, unclear, or missing	14	100	5.05
	<b>Sub-total</b>	<b>14</b>	<b>-</b>	<b>5.05</b>
<b>4. Treatment duration</b>	Duration of treatment too short	0	-	-
	Duration of treatment too long	0	-	-
	<b>Sub-total</b>	<b>0</b>	<b>-</b>	<b>-</b>
<b>5. Dispensing</b>	Prescribed drug not available	12	27.27	4.33
	Necessary information not provided	17	38.64	6.14
	Wrong drug, strength or dosage advised (OTC)	8	18.18	2.89
	Poor drug or strength dispensed	7	15.91	2.53
	<b>Sub-total</b>	<b>44</b>	<b>-</b>	<b>15.88</b>
<b>6. Drug use process</b>	Inappropriate timing of administration or dosing intervals	0	-	-
	Drug under-administered	0	-	-
	Drug over-administered	0	-	-
	Drug not administered at all	0	-	-
	Wrong drug administered	0	-	-
	Drug administered via wrong route	0	-	-
	<b>Sub-total</b>	<b>0</b>	<b>-</b>	<b>-</b>
<b>7. Patient related</b>	Patients use/take less drugs than prescribed or do not take the drug at all	57	36.08	20.58
	Patient uses/takes more drug than prescribed	18	11.39	6.50
	Abuse of drugs (unregulated overuse)	22	13.92	7.94
	The patient uses unnecessary drug	15	9.49	5.42
	Patients take food that interacts	0	-	-
	Patient stores drug inappropriately	31	19.62	11.19
	Inappropriate timing or dosing intervals	15	9.49	5.42
	The patient administers/uses the drug in a wrong way	0	-	-
	Patient unable to use the drug/form as directed	0	-	-
<b>Sub-total</b>	<b>158</b>	<b>-</b>	<b>57.04</b>	
<b>8. Other</b>	No or inappropriate outcome monitoring	28	100	10.11
	Other cause	0	-	-
	No obvious cause	0	-	-
	<b>Sub-total</b>	<b>28</b>	<b>-</b>	<b>10.11</b>
<b>Total</b>		<b>277</b>	<b>-</b>	<b>-</b>

DRPs: Drug-related problems

**Table 3.** Categorization and sub-categorization of interventions by research pharmacists

Primary domain	Intervention	Total	Domain proportion	Overall proportion
No intervention	No intervention	0	-	-
The prescriber level	The prescriber is informed only	19	20.88	5.01
	Prescriber asked for information	16	17.58	4.22
	Intervention proposed prescribing	27	29.67	7.12
	Intervention discussed with the prescriber	29	31.87	7.65
	<b>Sub-total</b>	<b>91</b>	<b>-</b>	<b>24.01</b>
At the patient level	Patient (drug) counseling	143	58.85	37.73
	Written information provided (only)	0	-	-
	The patient referred to prescriber	18	7.41	4.75
	Spoken to family member/caregiver	82	33.74	21.64
	<b>Sub-total</b>	<b>243</b>	<b>-</b>	<b>64.12</b>
At the drug level	Drug changed	0	-	-
	Dosage changed	0	-	-
	Formulation changed	0	-	-
	Instructions changed	16	35.56	4.22
	Drugs stopped	29	64.44	7.65
	A new drug is started	0	-	-
	<b>Sub-total</b>	<b>45</b>	<b>-</b>	<b>11.87</b>
Other intervention or activity	Other intervention	0	-	-
	Side effects reported to authorities	0	-	-
	<b>Sub-total</b>	<b>0</b>	<b>-</b>	<b>-</b>
<b>Total</b>		<b>379</b>	<b>-</b>	<b>-</b>

**Table 4.** Categorization of acceptance of research pharmacist's intervention proposals

Primary domain	Implementation of intervention proposals	Total	Domain proportion	Overall proportion
Intervention accepted	Intervention was accepted and fully implemented	211	65.12	55.67
	Intervention accepted implemented	54	16.67	14.25
	Intervention was accepted but not implemented	0	-	-
	Intervention accepted, implementation unknown	59	18.21	15.57
	<b>Sub-total</b>	<b>324</b>	<b>-</b>	<b>85.49</b>
Intervention not accepted	Intervention not accepted: not feasible	0	-	-
	Intervention not accepted: no agreement	7	43.75	1.85
	Intervention not accepted: other reasons	0	-	-
	Intervention not accepted: unknown reason	9	56.25	2.37
	<b>Sub-total</b>	<b>16</b>	<b>-</b>	<b>4.22</b>
Other	Intervention proposed, acceptance unknown	39	100	10.29
	Intervention not proposed	0	-	-
	<b>Sub-total</b>	<b>39</b>	<b>-</b>	<b>10.29</b>
<b>Total</b>		<b>379</b>	<b>-</b>	<b>-</b>

**Table 5.** Categorization of the DRP status after the research pharmacist's intervention proposal

Primary domain	Outcomes of interventions	Total	Proportion
Not known	Problem status is unknown	65	23.47
Solved	The problem has been totally solved	171	61.73
Partially solved	Problem partially solved	22	7.94
Not solved	Problem not solved, lack of cooperation of patient	0	-
	Problem not solved, lack of cooperation among prescriber	0	-
	Problem not solved; intervention not effective	19	6.86
	No need or possibility to solve problem	0	-
<b>Total</b>		<b>277</b>	<b>-</b>

All intervention proposals from the research pharmacist to attending physicians that were aimed at resolving identified DRPs were accepted. At the patient level, the research pharmacist's interventions principally consisted of health education, counseling, and psychotherapy. The research pharmacist emphasized medication adherence, drug storage, inappropriate timing or dosing interval, and irrational drug use. Patients were also discouraged from dual health-seeking behavior, i.e., patients combining traditional remedies with conventional pharmacotherapeutic management of epilepsy. Patients were also counseled about the need to undergo prescribed medical laboratory and radiological investigations.

We found that the doses and dosing of anti-seizure medicines prescribed as documented in the prescription sheets and patient case notes were appropriate in a large majority of the cases studied. Furthermore, there were no contraindications to the use of prescribed anti-seizure medicines in the cases studied. This is commendable, but expected, given that the study was conducted in a tertiary health facility with specialized services. However, therapeutic drug monitoring was not performed in any of the cases studied. The measurement and interpretation of serum antiepileptic drug concentrations can be beneficial for the treatment of uncontrollable seizures. Therapeutic drug monitoring enables a more decisive and effective optimization of therapy and disease management.<sup>12</sup> The lack of therapeutic drug monitoring in these facilities, as revealed in this study, may be due to the pervasive problem of the non-availability of the facilities required to conduct such investigations, a problem that appears to be common in resource-poor settings.

Studies have shown that clinical pharmacists can identify, resolve, and prevent clinically significant DRPs.<sup>13</sup> Interventions by the research pharmacist in this study resulted in the resolution of a significant proportion, about sixty-two percent, of the identified DRPs. This finding indicates the efficacy of PC interventions in identifying and resolving DRPs. This finding is in agreement with the results of a previous study in which it was found that PC interventions by pharmacists positively influenced clinical outcomes, including a reduction in the frequency of hospital re-admissions, length of patient stay in the hospital, and halting disease regression.<sup>13</sup>

Pharmacists, through pharmacotherapeutic monitoring, can detect the emergence of health problems and prevent the progression of co-morbidities.<sup>14</sup>

A previous study on the implementation of PC interventions on patients with HIV in primary healthcare found that pharmacist interventions were able to significantly reduce DRPs.<sup>15</sup> Other studies have also suggested that pharmacist interventions can reduce DRPs, particularly problems related to drug safety and adverse reactions.<sup>13,16-20</sup>

Acceptance of the research pharmacist's intervention proposals by prescribers indicates good interprofessional collaboration between physicians and clinical pharmacists. A fundamental requirement for creating collaborative practice systems between pharmacists and other healthcare providers is to appreciate the potential contributions of pharmacists to provide safer and more effective drug therapies for the management of various diseases and the overall good of the larger society.<sup>10</sup> Clinical pharmacists should be involved in the selection of suitable pharmacotherapeutic

agents for patients and should actively participate in clinical case discussions.<sup>13,15,17,21</sup> There is a compelling need for pharmacists to review all prescriptions before dispensing to patients. Furthermore, the therapeutic outcomes of direct patient care by pharmacists should be monitored and duly documented.<sup>4</sup>

A review of the available literature by Reis et al.<sup>8</sup> found that pharmacists' interventions were essential to improving the health of patients with epilepsy. These reports indicate that pharmacists' interventions can prevent drug therapy problems and improve adherence and response to anti-seizure medications. These studies also reveal significant achievements recorded by pharmacists and confirm that including pharmacists in the therapeutic team produces effective results for the success of pharmacotherapy and the quality of life of people with epilepsy.

### Study Limitations

The researchers could not determine the outcomes of some pharmaceutical interventions during the study. However, the results showed that the interventions were effective in resolving most DRPs.

### CONCLUSION

The most frequently encountered DRPs were patient related, which revolved around improper patient counseling and relaying medication information to caregivers rather than patients themselves. Most DRPs encountered were resolved following the acceptance of the pharmacist's PC interventions by the patients and attending physicians. PC interventions are effective in identifying and resolving DRPs.

### Ethics

**Ethics Committee 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. Date: 25: 04: 2016 & 11: 04: 2016 respectively).

**Informed Consent:** Informed consent was obtained from the participants prior to their recruitment into the study.

### Authorship Contributions

Concept: U.E., Design: U.E., C.M.U., Data Collection or Processing: U.E., N.I., Analysis or Interpretation: U.E., C.M.U., N.I., Literature Search: U.E., C.M.U., N.I., Writing: U.E.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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