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STUDY OF DRUG RELATED PROBLEMS IN COMMON NEUROLOGICAL CONDITIONS AND INTERVENTION BY CLINICAL PHARMACIST IN A TERTIARY CARE HOSPITAL

Nikitha Thomas, M. S. Gopika, Sradha Antony and Emily James *

Department of Pharmacology, Nirmala College of Pharmacy, Muvattupuzha - 686661, Kerala, India.

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Correspondence to Author:
Ms. Emily James

Associate Professor,
Department of Pharmacology,
Nirmala College of Pharmacy,
Muvattupuzha - 686661, Kerala,
India.

E-mail: emilyjames2001@gmail.com

ABSTRACT: Background: Drug-related problems are an ongoing, potentially harmful event that can affect the health of an individual. Various underlying health conditions and multiple drug uses are some of the factors contributing to drug-related problems (DRPs). This study aimed to determineDRPs in common chronic neurological conditions and intervention by clinical pharmacist in a tertiary care hospital, India. **Methods:** In this prospective study, the data of hospitalised neurological patients during December 2022–February 2023 were enrolled. Electronic medical databases and patient medical charts were used as data sources. Baseline characteristics were correlated with DRPs using Cramer's V correlation. The DRPs were classified using Pharmaceutical Care Network Europe (PCNE) Version 9.1. **Results:** A total of 300 patients were enrolled, in which the majority 83% had drug-related problems. The incidence of drug-related problems was found to be 0.27 cases per person per month. The most identified drug-related problem was found in the domain of treatment effectiveness, and the most identified cause belonged to the subdomain of drug use process. Most of the interventions proposed by clinical pharmacists were accepted by the health care professionals, and most of the DRPs were resolved. Drug-related problems were found to have a statistically significant correlation with polypharmacy (p value 0.001) and comorbidities (p value 0.001). **Conclusions:** The identification of drug-related problems and the recommendation of interventions by clinical pharmacists, together with the multi-disciplinary healthcare team, can optimise the use of medicines and improve health outcomes.

INTRODUCTION: Drug-related problems (DRPs) can occur at any stage, from prescription to follow-up treatment. Knowledge gaps, the number of drugs, patient age, and older patients with potentially inappropriate medications may indicate an increased risk for drug-related problems [1, 2].

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As per a cross-sectional study conducted by Noe Garin *et al.,* it was found that the occurrence of drug-related problems was mainly attributed to polypharmacy, renal impairment, allergies, and high BMI.

Elderly individuals may experience a high number of DRPs, particularly non-adherence to medications and the incidence of adverse drug reactions (ADRs), due to a decline in several organ functions, such as vision and memory, and changing pharmacokinetics and pharmacodynamics with normal ageing. This can lead to morbidity, death, and higher healthcare expenses [3].

DRPs are a significant contributor to emergency department visits, especially in older patients. The inclusion of a pharmacist-led medication review within a geriatric care team can identify and reduce DRPs. Medication review involves a systematic and thorough examination of a patient's medication with the goal of improving health outcomes; hence, it can result in shorter hospital stays, reduced ED visits, heightened patient satisfaction, and decreased health care costs [4, 5, 6].

The interaction between clinical pharmacists and physicians could be a crucial solution for DRPs. According to Lonowski's research, 90% of clinicians agreed that pharmacists' advice is clinically beneficial and that pharmacists have improved their understanding of the drugs they prescribe [7, 8]. As per a qualitative study conducted in Ireland, good collaboration between pharmacists and other health professionals depends on interprofessional trust and effective communication [9]. Clinical pharmacists can optimise drug therapy, adjust drug doses, promote drug adherence, monitor laboratory results, educate the patient, simplify the regimen, and find lower-cost alternative medications where appropriate [10]. The Pharmaceutical Care Network Europe (PCNE) classification tool has been suggested as a result of mounting evidence as a means of identifying the problems and causes of drug-related issues and facilitating their prompt prevention [11]. Syed *et al.* have revealed that the most frequent drug-related problems in the neurology departments were drug selection, dosage errors, drug interactions, and administration errors [12].

Drug-related problems in patients with chronic conditions like Stroke, epilepsy, and Parkinsonism can deteriorate their state. Age, polypharmacy, and different comorbidities are additional risk factors. Therefore, getting rid of drug-related problems is necessary for the patient's welfare. A medication management service that can improve the quality of care for each patient is the identification of drug-related issues. A viable method for enhancing treatment and patient-focused healthcare outcomes is to identify drug-related issues and suggest pharmaceutical actions. Therefore, lowering DRPs and increasing adherence can help to improve patient care quality, shorten hospital stays, and lessen the financial burden on patients.

MATERIALS AND METHODS:

Settings and Study Design: This prospective study was performed in the neurology department on hospitalised patients taking medicines for stroke, epilepsy, and Parkinsonism from December 1, 2022, to February 28, 2023, at the Caritas Hospital Kottayam, Kerala, a 700-bed tertiary care hospital in southern India. Ethical approval for this study was obtained from the Ethics Committee of Caritas hospital prior to its commencement (CH/EC/NOV/2023/031).

Sample size: Cochran's formula was adopted to identify the sample size for three months from the target population. Setting the standard score at 1.96, the precision level at 0.05, and the p value at 0.25, a minimum sample size of 288 patients was needed. Assuming that 100 patients were admitted to the neurology department each month, the total required sample size was determined to be at least 300 patients.

Study Subjects: Patients who were hospitalised in the neurology department taking medicines for stroke, epilepsy, and Parkinsonism with a duration of stay of more than 1 day were asked to participate in the study. Patients were informed about the study and given the opportunity to provide signed consent to it. Patients from all age groups were included in the study. The study excluded people who left without medical advice.

Data Collection: The inpatient files of suitable subjects were evaluated from the day of admission to the day of discharge. Patient characteristics and relevant medical data were collected from the Patient's medical records. Several demographic details, such as age, gender, polypharmacy, and comorbidities, were included. A direct patient interview was conducted to collect the subjects medical and medication history.

Description of Intervention: Clinical pharmacist took part in multidisciplinary ward rounds and provided interventions. They also identified drug related problems and classified it using PCNE classification system. The clinical pharmacist conducted proper medication reconciliation, checking the interactions of drugs from medication charts, monitoring Lab values, and identifying any untreated symptom or indication.

Transcription errors were also reduced by thorough checking of medication charts.

Classification system for DRPs: The identified DRPs were classified using Pharmaceutical Care Network Europe (PCNE) Version 9.1. It has 3 primary domains (P1-P3) and 7 grouped sub domains for problems, 9 primary domains (C1-C9) 43 grouped sub domains for causes and 5 primary domains (I0-I4) and 17 grouped sub domains for Planned Interventions, 3 primary domains (A1-A3) and 10 grouped sub domains for level of acceptance (of interventions) and 4 primary domains (O1-O3) and 7 grouped sub domains for the Status of the problem.

RESULTS:

Patient Characteristics: 300 individuals with common neurological conditions were admitted in the department of neurology during the 3 months study period (December to February) and among them 246 patients were having drug related problems (DRPs).

The mean age was 67 years old (61%) and 172 (57.3%) patients in the study were males, out of these cases 135 (78.4%) patients had DRPs. 128 (42%) of patients were females, in which 111 (86.7%) patients reported DRPs.

Among 240 patients had comorbidities, 215 of them (89.5%) had DRPs. 231 Patients had polypharmacy, in which 208 (90%) patients reported with DRPs. The most common type of neurological condition found were stroke (83.66%), followed by epilepsy (31.66%) and Parkinsonism (2.66%) **Table 1.**

TABLE 1: PATIENT DEMOGRAPHICS AND DISEASE CHARACTERISTICS

Number	Total	With DRP	Without DRP
Sex, Female	172 (57.3%)	135(78.4%)	37 (21.5%)
Sex, Male	128 (42%)	111 (86.7%)	17 (13.3%)
Age	(18-24) 7 (2.3%)	2 (28.5%)	5 (71.4%)
	(25-64) 110 (36%)	78 (70.9%)	32 (29.09%)
	(≥65) 183 (61%)	151 (82%)	32 (17.48%)
Smoke	51 (17%)	41 (80.39%)	10 (19.61%)
Alcohol	65 (21.66%)	54 (83%)	11 (17%)
Admission diagnosis			
Stroke	251 (83.66)	198 (79%)	53 (21%)
Epilepsy	41 (13.66%)	40 (98%)	1 (2%)
Parkinsonism	8 (2.66%)	8 (100%)	0 (0%)
Concomitant diseases			
Hypertension	177 (59%)	156 (88.1%)	21 (11.86%)
Diabetes mellitus	151 (50.33%	133 (88.07%)	18 (11.92%)
Dyslipidaemia	79 (26.33%)	66 (83.54%)	13 (16.45%)
Ischemic stroke	5 (1.66%)	5 (100%)	0 (0%)
Haemorrhagic stroke	3 (1%)	3 (100%)	0 (0%)
Coronary Artery Disease	49 (16.33%)	42(85.71%)	7 (14.28%)
Seizure	10 (3.33%)	10 (100%)	0 (0%)
Parkinson's Disease	9 (3%)	9 (100%)	0 (0%)
Hypothyroidism	19 (6.33%)	19 (100%)	0 (0%)
Others	80 (26.6%)	67 (83.75%)	13 (16.25%)

Identified Drug-related Problems: A total of 389 problems were identified, the most frequently recognized problems for the development of drug-related problems were drug Treatment Effectiveness P1 (51%) and Treatment Safety P2 (41%) **Table 2.**

Within the Treatment Effectiveness P1 category, the most identified sub domain was found to be no effect of drug treatment despite of correct use P1. 1 followed by untreated symptoms or indication P1. 3.

Causes of Drug-related Problems Identified: There were found to be 272 DRPs causes in all. The most frequently recognised causes for the development of drug related problems were drug use process C6 (62%) followed by drug selection C1 (30%). The most identified sub domain of drug use process C6 was found to be inappropriate timing of administration or dosing interval by a

health professional C6. 1(44.3%) followed by drug under administered by a health professional C6.2 (38.6%). Inappropriate drug according to guidelines/ formulary C1.1 (36.3%) and inappropriate combination of drugs, or drugs and herbal medications or drug and dietary supplements C1. 3(31.1%) was the major sub domain in the drug selection domain C1 **Table 2.**

Pharmacist Intervention to Solve the Drug-related Problems: A total of 246 interventions were proposed, most interventions identified at the prescriber level I1, followed by at the drug level I3. The most identified sub domain at the prescriber level (I1) was found to be intervention discussed with prescriber I1.4 (59.1%) and prescriber informed only I1.1 (40%). The most identified sub domain at the drug level I3 was drug paused or stopped I3.5 (82.4%) and drug started I3.6 (13.1%) **Table 2.**

Acceptance of Proposed Intervention: 84.1% of the intervention proposed were accepted and fully implemented A1.1 followed by intervention were accepted but not implemented A1.3 (15.85%) **Table 2.**

Status of the Drug Related Problems: Among 246 identified drug related problems, **Table 2** 65% of the problems totally solved O1.1 followed by problems partially solved O2.1 (17%) and problems not solved, lack of cooperation of prescriber O3.2 (16%).

TABLE 2: TYPES OF DRUG RELATED PROBLEMS, CAUSES, INTERVENTION AND ACCEPTANCE ACCORDING TO THE PHARMACEUTICAL CARE NETWORK EUROPE DRP TOOL VERSION V9.1

Primary domain	Number	Frequency (%)
Types of drug related problems		
Treatment effectiveness P1		
Effect of treatment not optimal P1.2	156	63.41%
Untreated symptoms or indications P1.3	42	17.07%
Treatment safety P2		
Adverse drug event (possibly) occurring P2.1	159	64.63%
Others P3		
Unnecessary drug treatment P3.1	10	4.07%
Unclear problem or complaint. Further clarification necessary P3.2	12	4.88%
Causes		
Drug selection C1		
Inappropriate drug according to the guidelines/formulary C1.1	23	9.35%
Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary supplements C1.3	21	8.54%
Inappropriate duplication of therapeutic group or active ingredient C1.4	6	2.44%
No or incomplete drug treatment in spite of existing indication C1.5	11	4.47%
Dose selection C3		
Drug dose too low C3.1	16	6.50%
Drug dose of single active ingredient too high C3.2	1	0.41%
Dose timing instructions wrong, unclear or missing C3.5	16	6.50%
Treatment duration C4		
Duration of treatment too short C4.1	1	0.41%
Drug use process C6		
Inappropriate timing of administration or dosing intervals by a health professional C6.1	59	23.98%
Drug under-administered by a health professional C6.2	51	20.73%
Drug over-administered by a health professional C6.3	14	5.69%
Drug not administered at all by a health professional C6.4	4	1.63%
Wrong drug administered by a health professional C6.5	2	0.81%
Patient related C7		
Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason C7.1	1	0.41%
Other C9		
Other cause C9.2	11	4.47%
Pharmacist interventions		
At prescriber level I1		
Prescriber informed only I1.1	96	39.02%

Intervention discussed with the prescriber I1.4	139	56.50%
At patient level I2		
Patient (drug) counseling 12.1	1	0.41%
At drug level I3		
Drug changed to … I3.1	1	0.41%
Drug changed to … I3.2	4	1.63%
Drug paused or stopped I3.5	94	38.21%
Drug started I3.6	15	6.10%
Other intervention or activity I4		
Other intervention I4.1	13	5.28%
Acceptance of intervention proposals		
Intervention accepted (by prescriber or patient) A1		
Intervention accepted and fully implemented A1.1	206	83.70%
Intervention accepted but not implemented A1.3	39	15.80%
Status of the DRP		
Not solved O3		
Problem not solved, lack of cooperation of patient O3.1	1	0.41%
Problem not solved, lack of cooperation of prescriber O3.2	6	2.44%
Problem not solved, intervention not effective O3.3	1	0.41%
No need or possibility to solve problem O3.4	39	15.85%

TABLE 3: CRAMER'S V CORRELATION OF DRPS IN VARIOUS SUBCLASSES OF POPULATION

Variable	Correlation	p-value
Comorbid	0.395	0.001
Polypharmacy	0.383	0.001
Gender	0.106	0.066
Alcohol	0.015	0.798
Smoking	0.019	0.743

DISCUSSION: There are only a few studies conducted in India regarding DRPs and their categorisation using the PCNE classification system. It was found that 0.25 of the patients had DRPs, which was comparable to a study done in a Chinese Neurology Department that similarly revealed 0.25 DRPs per patient [13]. The average number of DRPs was, however, less than that of the Iranian study (1.37 DRPs per patient) [14]. These variations in average no of DRPs could be due to difference in selection of department, sample size, duration of the study and so on. The identification of drug-related problems is a crucial area to focus on while treating the patient. It was found in our study the most drug related problems were visible in patients taking on medicines for Parkinsonism (100%) followed by epilepsy (98%) then stroke (79%). Similarly in a study of Drug related problems in Parkinson's disease conducted by Liu, Hui *et al* it was found that 83% of the population had DRPs [15].

The most common drug-related problems identified were in the category falling under drug treatment effectiveness (P1). No effect of drug treatment despite correct use (P1.1) was the common problem identified in treatment effectiveness. In the endeavour to cope with their impacts as well as avoid their occurrence, understanding the types of problems, which can be beneficial. In this study, drug selection and drug use process were the common causes for development of drug-related problems. Inappropriate drug according to guideline/formulary led to higher number of DRPs as this could have resulted by prescribing allergic drugs, drug contraindicated in renal failures and so on. There could be various reasons that can lead to this occurrence due to lack of communications with the patients and understanding about the use of a drug for a disease. Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary supplements also resulted in DRPs due to drug-drug interactions [16, 17].

Inappropriate timing of administration or dosing intervals by a health professional was seen during the study period. Lack of patient care might also occur for a variety of reasons, such as high patient load lack of communication between physician/patient or a lack of knowledge regarding the dosage of a specific prescription for a given disease condition. Most of the interventions proposed were accepted by the health Professionals and most of the drug-related problems were solved. However, in a study conducted by Pengpeng Liu *et al* treatment effectiveness was the most seen category of drug-related problems followed by treatment safety [18, 19]. In our study it was found that

majority of drug-related problems were in patients above or equal to 65 years of age (82%). Multiple factors, including pleuripathology and the resulting polypharmacy, complex dosing schedules, pharmacokinetic/ pharmacodynamics alterations, and functional/ cognitive abnormalities, put the aged at risk for drug-related problems [20, 21].

Correlation of drug related problems with various associated factors were done using Cramer's V correlation. From this statistical correlation method comorbidities and polypharmacy showed a medium correlation with drug-related problems (p value= 0.001) **Table 3.** Comorbidity is linked to the prescription of several medications, increasing the risk of exposure to unnecessary medications, the chance of duplicate therapies and drug-drug interactions, among other drug-related problems [22, 23]. These results are also in accordance with the findings of study conducted by Lea, Marianne *et al*, it was found that drug-related problems most frequently occur in people who are taking numerous medications.

In our study of patients with polypharmacy had the greatest number of drug related problems (90%). The complexity of multiple medication regimen could act as a threat for developing drug-related problems. The increased susceptibility to possible interactions between drugs and, as a result, to other drug-related issues may be explained by polypharmacy, comorbidity, and age-related physiological changes [24, 25]. In a study conducted by Koh, Yvonne *et al* it was demonstrated that polypharmacy increases the likelihood of drug-related issues.

This study has the following limitations 1. this study was limited to neurological disorders, 2. The study was conducted inpatient setting hence, a significant portion of patients in the outpatient setting were missed 3. Follow up regarding the status of DRP could not be done.

CONCLUSION: This study was conducted in patients of all age groups. DRPs were found in 246 out of 300 cases examined. At the end of the study most identified drug related problem was treatment efficacy and the most identified cause belonged to the subdomain of drug use process. This study also made clear how crucial it is to include clinical pharmacy services in multidisciplinary healthcare teams. Most medication-related problems can be avoided and prevented with the effective involvement of a clinical pharmacist in patient care.

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CONFLICTS OF INTEREST: Nil

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