A Clinical Pharmacist-led Approach on Reducing Drug Related Problems Among Patients with Neurological Disorders: An Interventional Study

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ABSTRACT

Background: Neurological disorders are common in the general population and the majority of patients have other chronic diseases, necessitating the use of multiple medications, which increases the incidence of drug-related problems (DRPs). Studies from different countries discovered an average of 0.29–1.45 DRPs per patient admitted into the neurology unit.
Objectives: To identify common DRPs and to evaluate the impact of clinical pharmacist's interventions in resolving the identified DRPs in patients with neurological disorders.
Methods: A prospective interventional study was conducted in the Department of Neurology in a tertiary care teaching hospital in Southern India, for a period of six months. Patients aged ≥18 years and had been hospitalized for >24 h, were intensively monitored until discharge for the occurrence of any DRPs and pharmacist interventions were provided. The identified DRPs were classified according to Hepler and Strand's Classification.
Results: A total of 310 prescriptions were reviewed, of which 174 patients (mean age 45.93 ± 2.49 years) experienced at least one DRP during their hospital stay. The average DRP per patient was found to be 1.75, with drug-drug interactions [254 (83%)] being the predominant DRPs, followed by adverse drug reactions [13 (4%)], and drug duplications [9 (3%)]. Most of the drug-drug interactions were pharmacokinetic [144 (56.69%)]. Hyponatremia [2 (15%)]; and nausea and vomiting [2 (15%)] were most commonly reported ADRs. All 306 DRPs involved active clinical pharmacist intervention, of which [275 (89.87%)] of pharmacists' interventions were accepted, which led to modification of the therapy.
Conclusion: Monitoring the use of drugs allowed the clinical pharmacist to detect DRPs and to suggest interventions that promote rational drug prescribing, therapy optimization and enhanced patient safety.

1. Introduction

The global epidemiological transition has shifted the focus from infectious diseases to non-communicable diseases (NCDs), and neurological disorders have emerged as a leading cause of disability and the second highest cause of mortality worldwide. The prevalence rates of the spectrum of neurological disorders from different regions of India ranged from 967 to 4070 with a mean of 2394 per 100,000 population, providing a rough estimate of over 30 million people with neurological disorders.[1,2]

Individuals diagnosed with neurological diseases are at an increased risk of developing drug-related problems (DRPs), which can result from the complex dosage regimens and potential drug interactions associated with many medications used to treat common conditions.[3] Inappropriate use of drugs used to treat neurological diseases has been linked to DRPs such as medication errors and adverse drug reactions. Studies from

different countries discovered an average of 0.29–1.45 DRPs per patient admitted into the neurology unit.[4] Moreover, around 5.0 to 10.0% of hospital admissions are estimated to occur due to DRPs, from which up to 60.0% are preventable.[5]

Through the provision of patient-centered pharmaceutical care, clinical pharmacy services (CPS) are intended to improve patient outcomes and reduce medication-related injury.[6] Clinical pharmacists collaborate with physicians in a multidisciplinary team to optimize medication prescribing by identifying, correcting, and averting DRPs in the hospital setting. The definition of clinical pharmacist interventions (CPI) is "any actions initiated by a pharmacist that directly result in a change in patient management or drug therapy.[7]" In numerous settings, clinical pharmacists have performed crucial roles in enhancing the quality of medication use. In North America, Australia, and Europe, the positive clinical and economic outcomes of their interventions have been well-established for decades.[8]

Clinical pharmacists continuously perform medication reconciliation from admission to discharge, and their interventions are defined by the categories of DRPs. Consequently, by reducing the incidence of DRPs, clinical pharmacy services can optimize the use of financial resources associated with the provision of inpatient health care. The most common interventions include starting a new medication, changing wrongly selected drugs, and optimizing drug dosing.[9] This integrated therapeutic approach is key in reducing the rate and pattern of DRPs in patients with neurological disorders. This study aims to estimate the DRP prevalence and to evaluate pharmaceutical care services provided by the clinical pharmacists in the Neurology unit of a tertiary teaching hospital.

2. Methods

A hospital-based prospective interventional study was conducted for six months at the Department of Neurology in Southern India. Patients of either gender aged 18 years or older who were admitted to the Department of Neurology and had a hospital stay of >24 h were enrolled in this study and their medication charts were reviewed for DRPs. Patients with cognitive impairment, terminally ill, or medico-legal status were excluded from the study. The study was approved by the Institutional Human Ethics Committee of the organization (Supplementary file).

Data collection was performed by reviewing treatment charts, laboratory reports, and through interviews with patients, caregivers, and healthcare professionals. Written consent was taken from eligible patients before enrolling them in the study. An integrated Clinical Pharmacist's intervention model was developed to assess the rate and patterns of DRPs and improve patient safety. This model included standard prescription checklist verification, medication reconciliation, and DRP assessment and management (Fig. 1).

Patients were prospectively followed, on day-to-day basis, from the date of hospital admission till the date of discharge. During the routine patient care process, a comprehensive medication assessment of patients' treatment charts was performed to identify any DRPs. The identified DRPs were reviewed and classified based on Hepler and Strand's medication-related problems: untreated indications, improper drug selection, sub therapeutic dosage, failure to receive medication, overdosage, adverse drug reactions, drug interactions, and drug use without indication.[10] DRPs not belonging to the above mentioned classification were categorized using other relevant evidence from medical literature and clinical practice. All reported adverse

drug reactions (ADRs) were assessed for causality using World Health Organization-Uppsala Monitoring Centre causality assessment scale[11] and Naranjo's algorithm,[12] preventability using Schumock and Thornton scale,[13] severity using modified Hartwig and Siegel scale,[14] and predictability based on prior exposure to the suspected drugs or based on the literature incidence of the suspected ADRs.[15] Drug–drug interactions were categorized according to the Lexicomp severity rating and clinical importance into four categories; "minor" in which no intervention is required; "moderate" where monitoring of drug therapy is required and "major" denotes interactions with a high potential for severe adverse outcome.[16]

The identified DRPs were managed by clinical pharmacists, who provided recommendations for each medication order to the healthcare team. Descriptive statistics were used to represent the study results, and the rate of acceptance of the pharmacist's intervention by other healthcare professionals was calculated.

2.1. Predictors

Logistic regression to determine the odds ratio (OR) at 95% confidence interval was measured to calculate the predictors for DRP occurrence. Variables such as gender, age, length of hospital stay, and number of medications were considered for the assessment of predictors using JMP Pro 16 software. The statistical significance was considered as $p < 0.05$. Further, all the categorical variables were represented as numbers with percentages wherever applicable.

3. Results

3.1. "Demographic characteristics of the study participants

A total of 310 eligible patients were enrolled in the study, with the majority being male (56%). The mean age of the participants was 45 years, as shown in Table 1.

The study population consisted of a significant number of patients (26.45%) diagnosed with epilepsy, followed by cardiovascular accidents (CVA, 20.32%). The primary diagnosis of the study population is shown in Fig. 2. Out of the total 310 patients, the majority (80.96%) did not have any chronic disease conditions, while 10.96% had hypertension, followed by 6.45% with diabetes mellitus, 1.93% with hypothyroidism, and 1.61% with cardiovascular diseases.
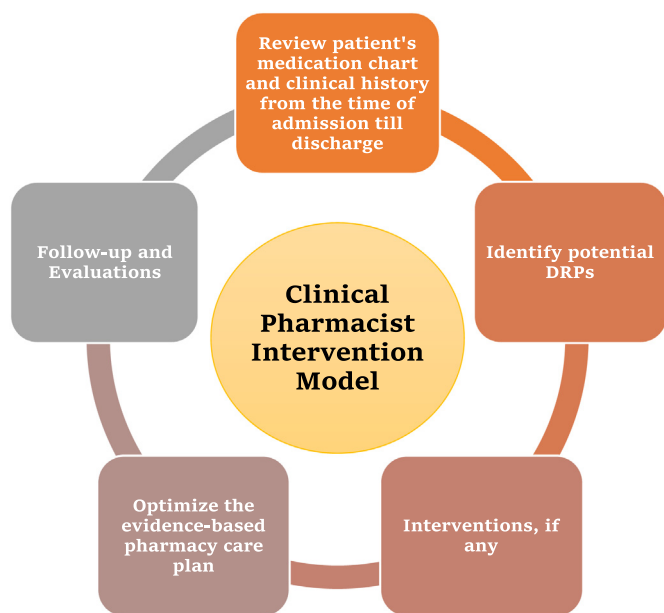

Fig. 1. Clinical Pharmacist's Intervention Model.

Table 1

The Demographic Characteristics of the Study Population.

| Demographic Characteristics		Number of Study Participants (%) $N = 310$
Gender	Male	175 (56.45)
	Female	135 (43.54)
Age (In years)	18–20	24 (7.38)
	21–40	105 (33.87)
	41–60	110 (35.4)
	61–80	70 (22.56)
	>80	1 (0.32)
	Mean ± SD	45.93 ± 2.49
No. of Comorbidities	0	251 (80.96)
	1	41 (13.22)
	2	14 (4.51)
	3	4 (1.29)
No. of Drugs Prescribed	1	88 (28.38)
	2	89 (28.70)
	3	60 (19.35)
	4	34 (10.96)
	≥5	39 (12.58)
Length of Stay (In days)	1–2	26 (8.38)
	3–5	146 (47.09)
	6–10	119 (38.38)
	>11	19 (6.12)
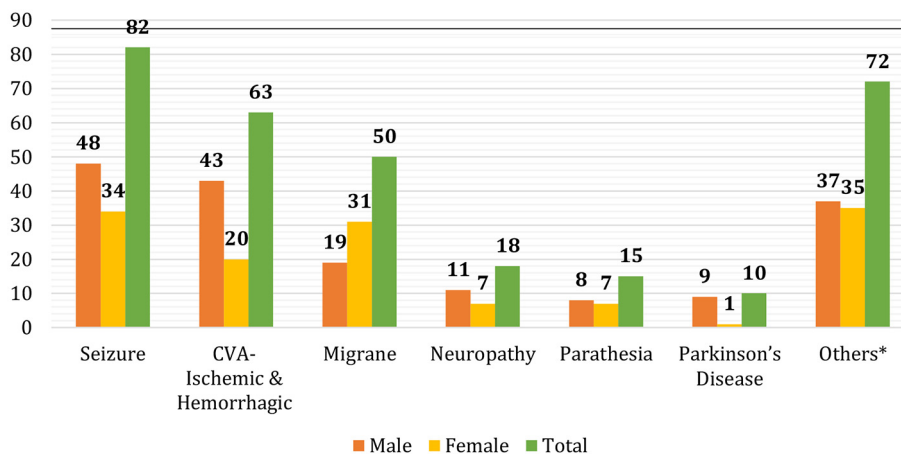
Fig. 2. Primary Diagnosis of the Study Population. * Cervical Spondylitis (8), Optic Neuritis (7), Acute Inflammatory Demyelinating Polyradiculopathy (5), Bell's Palsy (4), Cervical Radiculopathy (2), Gullian Barre Syndrome (1), Chronic Cranial Pachymeningitis Meningitis (1), VitaminB12 Deficiency (1), Idiopathic Intracranial Hypertension (1), Trigeminal Neuralgia (1), Brachial Plexopathy (1) and Acute Motor Sensory Axonal Neuropathy (1).

Number of Drug-Related Problems (DRPs) per patient:

During the study period, it was found that 56% of the study population experienced at least one DRP during their hospital stay. The average number of DRPs per patient was 1.75, with 54.02% of patients experienced one DRP, and 29.88% experienced two DRPs.

Drug-Related Problems:

A total of 306 DRPs were identified and classified according to Hepler and Strand's classification[7] during the study period. The predominant DRP was drug-drug interactions [254 (83%)], followed by adverse drug reactions [13 (4%)] and drug duplication [9 (3%)]. The various drug-related problems identified during the study are presented in Table 2. [189 (61.76%) DRPs were experienced by females and [117 (38.23%) by males.

3.2. Drug-drug interactions

A total of 254 drug interactions were identified during the study period. The majority of drug interactions identified were major [123 (48.42%)], followed by moderate [108 (42.51%)], and minor [23 (9.05%)] in nature.

Identified DDIs were further classified according to pharmacokinetic and pharmacodynamic. Of the 254 reported DDIs, the majority were pharmacokinetic interactions [144 (56.69%)], wherein [113 (78.47%)] were interactions due to changes in metabolism. Among the pharmacodynamic interactions [110 (43.3%)], [50 (45.45%)] were synergistic. The detail of the types of DDIs reported is presented in Fig. 3.

The most common co-prescribed medications with significant drug-drug interaction potential were Amitriptyline and Domperidone and Amitriptyline and Atorvastatin, which were found 9.05% and 3.15% of drug interactions, respectively (Table 1- supplementary file).

3.3. Adverse drug reactions

During the study period, 13 adverse drug reactions were identified and reported. The ADRs identified during the study period are presented in Table 2 -supplementary file.

Causality Assessment of ADRs:

The majority of the ADRs were classified as Possible [7 (54%)] in nature, followed by Probable [6 (46%)] in nature, according to the WHO-UMC causality assessment scale.

Severity Assessment of ADRs:

The severity of the reported ADRs was found to be mild level 2 [5 (38.46%)], followed by moderate level 3 [3 (23%)], moderate level 4 (b) [3 (23%)], and the least being moderate level 4 (a) [2 (15.38%)].

Preventability and Predictability Assessment of ADRs:

The majority [6 (46.15%)] of the ADRs were found to be 'probably preventable' followed by 'definitely preventable' [4 (30.76%)]. The predictability of the reported ADRs was assessed by using a predictability scale, it is observed that [9 (69.23%)] ADRs were 'predictable'.

Outcomes of reported ADRs:

The majority of the patients [9 (69.23%)] recovered, and [4 (30.76%)] recovering. The severity, preventability, predictability, and outcome of the reported ADRs are shown in Table 3- supplementary file.

3.4. Other DRPs

A total of [9 (2.94%)] drug duplications were found wherein Atorvastatin (33.33%) was the drug most commonly duplicated. Out of [8 (2.61%)] drug overdoses, Thiamine was the predominant one. Anaemia (56.14%) was the most common untreated indication found in the study (Table 4 supplementary file).

3.5. Rate of acceptance of pharmacist interventions by health care professionals

The rate of acceptance of pharmacists' interventions regarding untreated indications, improper selection of drugs, drug duplication, overdose, drug-drug interactions, and adverse drug reactions was [275 (89.87%)] among a total of 306 identified drug-related problems.

Changes in the time of administration (36%) was the most common intervention suggested by the clinical pharmacists followed by dosage adjustments (24%), cessation of drug (21%) (Table 3). [46 (15.03%)] interventions provided were considered to be of major significance, [148 (48.36%)] as moderate and [112 (36.6%)] as minor. The pharmacist interventions provided for all the 306 DRPs identified are shown in supplementary file table 5.

Table 2
Categorization of DRPs Identified.

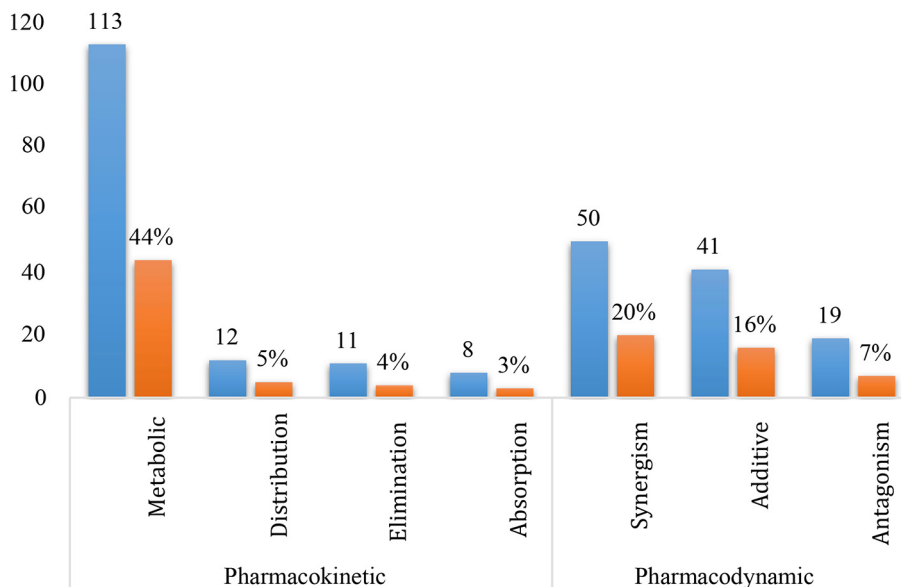| Category of DRPs	No. of DRPs (%) $n = 306$
Drug interactions	254 (83)
Adverse drug reactions	13 (4.24)
Drug duplication	9 (2.94)
Overdose	8 (2.61)
Untreated indication	7 (2.28)
Improper drug selection	6 (1.96)
Sub-therapeutic dosage	5 (1.63)
Drug use without indication	4 (1.30)
Total	306 (100)

Fig. 3. Types of Drug-Drug Interactions.

Table 3
Pharmaceutical Care Services Interventions Offered by Clinical Pharmacists.

Sl. No	Suggestions	Number (%)
1	Change in time of administration	110 (36.03)
2	Change in drug dose	69 (22.55)
3	Cessation of drug	63 (20.37)
4	Addition of drug	33 (10.9)
5	Substitution of drug	22 (7.18)
6	Change in route of administration	9 (3.02)

Predictors:

Age [OR 1.0155, 95% CI 1.0017–1.0295 (p = 0.0267)] and number of medications [OR 1.3208. 95% CI 1.1028–1.5817 (p = 0.0025)] were found to be the predictors for the occurrence of DRP.

4. Discussions

In this study, a patient-centric Clinical Pharmacists' intervention model was developed to evaluate the patterns and rates of various drug-related problems. The identified drug-related problems (DRPs) were classified according to the Hepler and Strand classification of DRPs. The prevalence of the spectrum of neurological disorders in the country is alarming and an average of 1.75 DRPs per patient was identified. During the study period of six months, the researchers proactively identified and managed a total of 306 DRPs during daily regular activities in the neurology ward. Similarly, Lenssen R et al. also reported an average rate of DRP to be 0.15–2.9 DRPs per patient,[17] this incidence of DRP is greater than the reported rate (2.1%) by Ali MAS et al. in a Chinese neurology care unit employing prospective electronic prescription review but lower than the global medication incidence rate of 7% per medication order reported in hospital inpatients.[18] The higher number of nine average drugs per patient explains this. This also showed that the patients have a significant need for pharmaceutical care.

In the current study, it was found that there was a positive association between the number of drugs prescribed to the study participants and the occurrence of various drug-related problems. A similar observation was made by Namaziet al,[19]. where the incidence of drug interactions occurring in patients receiving more than five drugs was 6.91 times higher than those receiving less than five drugs (P < 0.001, 95% CI = 4.23–11.27).

The majority of DRPs were drug-drug interactions [254 (81%)] in the study, in contrast to other studies in which drug interactions caused 2.9% to 17% of all DRPs, wherein the drugs such as Aspirin (39.20%), Heparin (40.50%) and Clopidogrel (19.50%) were associated with the DDIs.[20] The current study findings reflected that the majority of DDIs were caused by Amitriptyline [83 (32.68%)], a tricyclic anti-depressant, followed by Aspirin [47 (18.50%)]. Since most of the drugs prescribed for neurological disorders are potent enzyme inducers or inhibitors (Phenytoin, Valproic acid, Amitriptyline, Carbamazepine), metabolic changes in the pharmacokinetic parameters of the drugs were responsible for the majority of drug-drug interactions.

Our study showed that age (p = 0.0267) and, number of drugs used (p = 0.0025) were the predictors associated with the occurrence of DRP. Drugs such as Carbamazepine, Phenytoin, Phenobarbital, Valproic acid, and benzodiazepines, which are used to treat epilepsy, have significant potential for the occurrence of DDIs and adverse effects, thus lowering the quality of life in patients. As a result, DDIs associated with the use of anti-epileptic medications were widespread.

Except Amitriptyline, which is an anti-depressant, the majority of DRPs were caused by Aspirin, Clopidogrel, Domperidone, and Atorvastatin, which are not specifically given for the treatment of neurological diseases. Analgesics, anti-platelet drugs, anti-convulsant, and lipid-lowering medications were most often implicated in causing DRPs in a previous study done by Taegtmeyer AB et al. to detect the DRPs in the neurology inpatients of a large Swiss University Hospital.[21]

Typically, clinical pharmacists recommended dosage adjustments, additions, cessations and drug substitutions. Patients with renal/hepatic impairment or who were underweight accounted for the majority of dosage modifications. In cases of untreated prevalent diseases, such as anaemia, the drug was suggested for addition. Similar observations was observed in a study conducted by Rodrigues JP in a Brazilian tertiary care hospital.[22]

Acceptance of pharmacist interventions accounted for over 89.87% of the cases. However, a study by Parthasarathi G et al. observed that the decision-making by clinical pharmacists and the overall acceptance rate by other healthcare professionals was 90%.[23] The decision-making and their level of involvement had shown interesting results that potentially optimize the betterment of patient care.

Therefore, the study may reflect proper prescribing practices and awareness of guidelines and recommendations for neurological disorders among the practitioners. This also shows that clinical pharmacist services have a good impact on the neurology specialty and that clinical pharmacists

can help identify drug-related problems with drugs administered for non-neurological disorders.

However, the study had some limitations. The impact of clinical pharmacist interventions on reducing the number of hospital admissions or financial savings was not evaluated because of the unavailability of documented data and the long-term impact of Pharmacists' interventions on patient outcomes was not evaluated. Also, this study was only conducted in the neurology ward of one teaching hospital where patients with certain disorders and particular medications were admitted, which may impact the generalization aspect of the obtained results.

5. Conclusion

This study highlights the importance of detecting and avoiding drug-related problems (DRPs) in patients with neurological disorders. The active involvement of a unit-based clinical pharmacist in therapeutic interventions, combined with a high rate of acceptance by other healthcare professionals, leads to improved patient care and rational drug prescribing. The findings emphasize the critical role of clinical pharmacists in ensuring high-quality and safe patient care.

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Ethical approval

The study proposal was made in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of JSS Medical College, Mysuru (Letter No.: JSSMC/ IEC/17112021/ 11 NCT / 2021–22).

Declaration of Competing Interest

The authors declare that there are no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rcsop.2023.100302.

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