

Assessment of Drug Related Problems in Stroke Patients Admitted to a South Indian Tertiary Care Teaching Hospital

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ABSTRACT

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Introduction: Drug related problems contribute to patient's morbidity, mortality and decreased quality of life. Drug related problems can occur at any stage of prescribing, transcribing, dispensing and administration of medications. Identifying and resolving the drug related problems will improve the patient's safety and therapeutic outcomes. **Objective:** To study the rate, types, pattern, and clinical significance of drug related problems in stroke patients. **Methodology:** A prospective study was conducted in the medicine and neurology wards of a tertiary care hospital over a period of six months from November 2011 to April 2012. Necessary demographic and clinical data was collected from the case records. The treatment data was analyzed to determine the rate, pattern, clinical significance, and outcomes of DRPs in stroke patients. **Results:** A total of 80 DRPs were identified in 108 patients. The frequency of drug related problems was 1.54 per patient. The highly reported drug related problem was drug interactions (25.0%) followed by drug use without indication (15.0%) and adverse drug reactions (15.0%). Majority interventions (97.9%) were accepted by the health care professionals. **Conclusion:** Early detection and intervention of drug related problems may improve the therapeutic outcomes in stroke patients. Developing and adopting policies regarding the drug administration, dispensing and prescribing would minimize the drug related problems in stroke patients.

Keywords: Drug related problems, Stroke, Clinical Pharmacist.

INTRODUCTION

The main objective of medication use in any disease is to optimize drug therapy with minimum safety related problems within the frame work of pharmaceutical care plan.¹ The goal of pharmaceutical care is to optimize the drug therapy, achieve positive clinical outcomes within realistic economic expenditures and improve patient's health related quality of life.² Availability of new drug therapies and increased use of medications may potentially increase the risks for patients to iatrogenic adverse drug events in the hospitals. Iatrogenic adverse events are important for consideration because they not only prolong the hospital stay but also increase the health care expenditures.³

The objective of prescribing drugs to patients is either for prophylaxis or diagnosis of medical conditions, or to treat a clinical condition. Drugs play an important role in the management of diseases. A Drug related problem (DRP) is defined as an any event or circumstance involving drug treatment that interferes or potentially interferes with the patient achieving an optimum outcome of medical care.³ Cipolle classified drug related problems in to eight types, such as

- 1) Untreated indication
- 2) Drug use without an indication
- 3) Improper drug selection
- 4) Sub therapeutic dosage
- 5) Over dosage
- 6) Medication error/noncompliance
- 7) Drug interactions, and
- 8) Adverse drug reactions.⁴

Occurrence of a DRP may prevent or delay in achieving desired therapeutic goals. Drugs if wrongly prescribed may cause negative health outcomes due to Drug related problems (DRPs) and pose significant challenge to health care providers and may contribute to morbidity, mortality and lead to a negative quality of life (QoL) in patients.³ Drug related problems may arise at all stages of the medication process from prescription to follow – up of the treatment. Lack of follow-ups and reassessment of medical treatment is also a major problem contributing for DRPs.⁵

Pharmacists can play an important role in identifying drug related problems (DRPs), resolving actual DRPs and preventing potential DRPs through pharmaceutical care practices. An actual DRP is an event that has already occurred in a patient, whereas a potential DRP is an event that is likely to develop if pharmacists do not make any appropriate

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interventions. Studies have shown that majority (50-80%) of drug related problems can be prevented.³ Data suggest that there is a significant need for the improvement in the use of drugs for hospitalized patients as medication related adverse events has been identified as contributing to negative clinical and economic outcomes including hospitalization and increased hospitalization costs.⁶

Although pharmacotherapy can treat diseases and improve the well-being of patients, its benefits may be compromised due to drug related problems. Therefore it is important to assess drug related problems resulting in serious injury or death and analyze whether improvement in the prescribing practices can be made to reduce the likelihood of similar events occurring in the future.

Stroke is the second most common cause of death worldwide and is the leading cause of long-term disability in adults, with 90% of survivors having residual deficits. Stroke incidence increases with age (especially after age 55), hypertension and dyslipidemia.⁷ Physicians continue to seek ways to achieve better functional recovery in stroke patients and reduce the devastating impact of stroke on the society. Several studies have shown that patients with stroke are among those at high risk for the development of DRPs due to elderly age, comorbidities and poly pharmacy. Therefore, identifying and resolving DRPs is an important priority for health care professionals for improving the therapeutic benefits and health related quality of life in stroke patients.⁸

Participation of pharmacists in patient care (pro-active approach) was proven to improve medication adherence, while decreasing prescribing errors. This service has decreased health care costs, morbidity and mortality and improved the health related quality of life. Studies have demonstrated the consistent benefits of pharmacist involvement in the management of hypertension and dyslipidemia, which are considered two major modifiable risk factors in stroke prevention. Provision of clinical pharmacy services ensures that medicine therapy is optimum, safe, cost-effective and individualized and helps in resolving drug related problems.⁹

METHODOLOGY

The present study was a prospective study and conducted in the general medicine and neurology wards of 1,200 bed South Indian tertiary care teaching hospital. The study was approved by Institutional Ethics Committee. A suitable data collection form was designed to collect demographic details of patients such as age, sex, and weight, date of admission, date of discharge, reasons for admission and diagnosis, medications used including name of the drug, dose, route, frequency of administration, duration and indication for use, type of drug related problem (DRP), brief description of DRP, suggestions

provided, significance of DRPs, level of clinical pharmacist involvement in the clinical decisions and outcomes of identifying DRPs. Demographic and clinical data was collected for all patients meeting the inclusion criteria. The treatment initiated was analyzed for drug related problems. All the DRPs identified were documented and reviewed on a daily basis. The identified DRPs were categorized as per Cipolle's classification in the documentation form. In the assessed DRPs, where required the information was provided to the prescribers with suitable strategies to resolve the DRP such as dose adjustment, drug interactions, and adverse drug reactions. Later, the data was then entered in to Microsoft access sheet for the storage, easy retrieval and analysis of results. Any changes in the patient's therapeutic management, including change in medication orders and other relevant information such as lab data and patient's daily clinical progress were noted and updated on daily basis. The acceptance level of the health care professional for the particular DRPs was also considered as either accepted or not accepted. Similarly a change in drug therapy if any was also noted. The suggestion provided for a particular DRP was categorized into the following categories: Change in drug dose, Change in dosage form, Addition of drug, Cessation of drug, Substitution of drug, Change in route of administration, Change in frequency of administration, Change in duration of therapy and others.

RESULTS AND DISCUSSION

The study was conducted in a tertiary care teaching hospital, where 45839 patients were admitted during the study year. Among them, 554 (1.2%) were stroke patients and received medicines like anti platelet agents, statins, low molecular weight heparin, antihypertensives, oral hypoglycemic agents etc. with an average of 4-5 medicines per patient. The demographic details, clinical details, therapy given, types of drug related problems, were analyzed from the data collected. During the study period (November 2011 to April 2012) 108 stroke patients were admitted. Among the stroke patients admitted, 93(86.1%) patients were admitted with ischemic stroke and 15 patients (13.9%) were admitted with hemorrhagic stroke. Out of 93 ischemic stroke patients, 59 patients (63.4%) were males and 34 patients (36.5%) were females. Similarly out of 15 hemorrhagic stroke patients, 12 patients (80%) were males and 3 patients (20%) were females. Majority (25.0%) of the patients were in the age group of 60-69 years. Among the study population, 39.8% of patients were diagnosed to have one co-morbidity and 17.6% of the patients were with two comorbidities and two patients (1.8%) were having three comorbidities and 40% of the patients were not having any co morbidity. During the hospital stay, majority (88.0%) patients received six to ten drugs on an average. Demographic characteristics of the stroke patients are presented in Table 1.

Table 1: Demographic details of the Stroke Patients

Patient Characteristics	Number (%) (N=108)
Age (years)	
<40	8(7.4%)
40-49	20(18.5%)
50-59	23 (21.2%)
60-69	27(25.0%)
70-79	20 (18.5%)
80-89	8 (7.4%)
90-99	2(1.9)
Sex	
Male	74(68.5%)
Female	34 (31.5%)
Number of medication received	
1-5	13 (12.0%)
6-10	95 (88.0%)
Number of co-morbidities	
0	43 (39.8%)
1	43 (39.8%)
2	19 (17.6%)
3	02 (1.8%)
Length of hospital stay (in days)	
1-2	1(0.9%)
3-5	34(31.5%)
≥6	73(67.6%)

A total of 80 DRPs were identified in 108 patients during the study period. The frequency of DRP was 1.4 per patient. Among the 80 DRPs, 62 (77.5%) were identified in male patients and 18 (22.5%) DRPs were identified in female patients.

Types of drug related problems identified (n=80):

The most common drug related problem was found to be drug interaction which accounted for 25.0% (n=20) of total DRPs followed by drug use without indication [n=12 (15.0%)] and adverse drug reaction [n=12 (15.0%)]. Types of DRPs are summarized in figure 1.

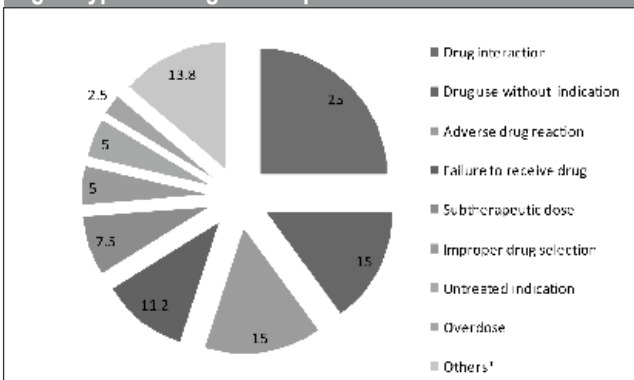
Drugs involved in various drug related problems

The details of medications involved in DRPs with ATC code are presented in Table 2.

Adverse Drug Reactions: Causality Assessment

Causality assessment of ADRs was analyzed. Among the identified ADRs, all the ADRs belong to 'Probable' category on WHO scale.

Fig. 1:Types of drug related problems identified



*Drug duplication [n=2(18.2%)], Medication errors [n=8 (72.7%)] Irrational use of antibiotics [n=1 (9.1%)]

Severity of ADRs:

Majority (83.3%) of the observed ADRs was found with 'Mild' in severity, 16.7% was 'Moderate' and none of the ADRs were found to be 'Severe'.

Preventability of ADRs:

All the identified ADRs (100%) were 'Not preventable' and none of them were 'Probably preventable' and 'Definitely preventable'

Suggestions provided:

Among the suggestions provided, majority of the suggestions were provided to Post graduate (PG) medical students [n=60(75.0%)] followed by physicians [n=9(11.2%)] and nurses [n=7(8.8%)]. And very few suggestions were provided to interns [n=4(5.0%)] The details of suggestions provided are presented in Figure 2.

Acceptance rate of DRPs identified:

The acceptance rate of DRPs identified was found to be 97.0% (n= 80). The details of acceptance rate of DRPs are presented in Figure 3.

Fig. 2: Suggestions Provided

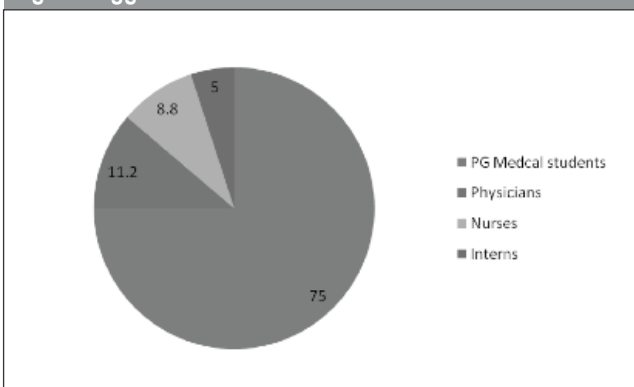
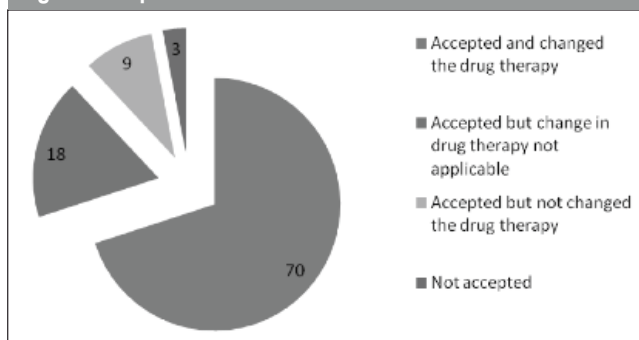


Table 2: Drugs involved in various drug related problems

Types of DRPs	No. of DRPs (n=248)	Drugs involved	ATC code	No.
Drug use without indication	12	Domperidone	A03FA03	3
		Ondansetron	A04AA01	3
		Pantoprazole	N03AB05	3
		Piperacillin+tazobactam	A02BC02	1
		Paracetamol	J01MA12	1
		Tramadol	B03AA07	1
Untreated indication	4	Anemia		1
		Cough with expectoration		2
		Vomiting		1
Subtherapeutic Dose	6	Amlodipine	A10AB01	2
		Metoprolol	C07AB02	2
		Telmisartan	C09CA07	1
		Nimodipine	C08CA06	1
Overdose	2	Rabeprazole	A02BC04	1
		Ranitidine	A02BA02	1
ADR	12	Amlodipine	C08CA01	4
		Ciprofloxacin	J01MA02	1
		Atorvastatin	C10AA05	2
		Insulin	A10AB01	2
		Ceftriaxone	J01DD04	1
		Piperacillin+tazobactam	J01CA12	1
Drug-drug Interactions	20	Aspirin	N02BA01	2
		Clopidogrel	B01AC04	2
		Enoxaparin	B01AB05	4
		Rabeprazole	A02BC04	1
		Atorvastatin	C10AA05	1
		Oxcarbazepine	N03AF02	1
		Insulin	A10AB01	3
		Glimepiride	A10BB12	1
		Metformin	A10BA02	1
		Metoprolol	C07AB02	1
		Diclofenac	M01AB05	1
		Lisinopril	C09BA03	1
		Phenytoin	N03AB02	1
		Improper drug selection	4	Ramipril
Rabeprazole	A02BC04			1
Ondansetron	A04AA01			2
Failure to Receive drugs	9	Iron preparation	B03AA07	1
		Multivitamins	P02CA01	1
		LMWH	A11AA03	1
		Paracetamol	A01AC03	1
		Phenytoin	N03AB02	1
		Ceftriaxone+sulbactam	A07EA06	1
		Albendazole	J01DA63	1
		Amlodipine	R03DA11	1
Ciprofloxacin	J01DD04	1		
Medication errors	8	Aspirin	N02BA01	2
		Clopidogrel	B01AC04	2
		Atorvastatin	C10AA05	2
		Pantoprazole	A02BC02	1
		Mannitol	B05BC01	1
Irrational use of antibiotics	1	Ciindamycin	D10AF10	1
Drug Duplication	2	Pantoprazole	A02BC02	1
		Clopidogrel	B01AC04	1

Fig. 3: Acceptance rate of recommendations

DRPs are relatively common in hospitalized patients and can result in patient morbidity mortality and increased treatment costs. More the number of drugs used, more will be the number of clinical/pharmacological risk factors significantly contribute to the risk for DRPs. In India, clinical pharmacy service is an emerging discipline. Clinical pharmacy service is to optimize the patient outcomes by working in concordance with prescriber and patient. Research studies have shown that the clinical pharmacy activities reduce the drug related problems relating to hospitalization²⁰, probability of readmission and total cost of the drug therapy³.

The aim of the present study was to assess the DRPs in prescriptions given for Stroke patients as stroke is a major source of increased mortality and morbidity¹⁴. Medicine and Neurology departments were chosen for the study owing to the potential for admission of stroke patient population and with multiple comorbidities receiving poly pharmacy.

Among 108 stroke patients followed during the study period, a total of 80 DRPs were identified and assessed. Out of 108 patients, 68.5% were males and 31.5% were females. The main reason for this high incidence in male population is due to male gender predominance in the stroke patients due to various risk factors and co morbidities compared to the female population. The total number of DRPs, were obtained more in the male population. This observation is supported with the demographic reports of the study conducted by Ganachari M S et al⁵, cited a predominance in male gender over female gender. Another study conducted by Madhan Ramesh et al¹⁵ has shown similar predominance of males over females. The incidence of DRPs were high (25.0%) in patients aged between 60-69 years. Among the potential contributing factors of DRPs, the association between poly pharmacy and the incidence of DRPs has been studied and documented.¹⁶ In 95.0% of cases DRPs were seen in patients receiving more than 6 drugs. This observation is supported with a 2002 national survey indicated that 50% of the overall population took 5 or more medications and developed DRPs.¹⁷ In another study conducted by H.A.M. Vinks, it was

found that DRPs may be frequently occur in adults over 65 years of age using six or more drugs concomitantly.¹² This clearly indicates that geriatric age and poly pharmacy are the potential risk factors for developing DRPs in Stroke patients. The more frequent use of drugs by the elderly can be explained by the high prevalence of multiple morbidities and the increased availability of pharmacotherapeutic options.

Most of the DRPs observed in the study resulted from drug interactions (25.0%). It was followed by drug use without indication (15.0%) and adverse drug interactions (15.0%). This observation is supported with the study conducted by Yvonne Koh in which potential drug-drug interactions accounted for a substantial amount of potential drug toxicity (34.8%).¹⁶ This study is contrasted with the study conducted by H.A.M. Vinks found that the most frequently occurring potential DRPs were drug use without indications. Drug use without indication was defined if the indication for a certain prescription was disputable or not evidence-based anymore.¹² In the present study the therapeutic agents most implicated were anticoagulant (Enoxaparin), anti-inflammatory agents (Diclofenac), and antiplatelet agents (Aspirin and Clopidogrel). This is consistent with the published study conducted by Yvonne Koh, citing that the average number of drug-drug interactions involving anticoagulants were higher than other drug groups. As drug-drug interactions can affect patient's clinical outcomes, quality of life and contribute to unnecessary health care costs, the high prevalence rate (25%) in this study would make this as an important area requiring further investigation and the future pharmacist should focus on reviewing patients' medication charts and checking for potential drug interactions regularly.¹⁶ In a German study, conducted by Langerbake C et al¹⁷, 'drug use without indication' was found to be second highest which is again comparable with our results. The study conducted by Madhan Ramesh et al¹⁵ has also shown a high incidence (18%) of drug use without indication. Probable reasons for this DRPs may be due to prophylactic reasons or lack of therapeutic guidelines in the hospital indicating a need for the initiation of clinical pharmacy services and development of therapeutic guidelines.

Besides the undesirable clinical consequences for the patients, ADRs also pose a significant financial burden to the health care system.¹⁶ Out of 108 patients 12 ADRs (15%) were identified. The most common ADRs involved were amlodipine induced constipation (33.3%) followed by atorvastatin induced myopathy (16.7) and insulin induced hypoglycemia (16.7). Among the risk factors, elderly age has been associated with increased risk for developing ADRs. The association between the poly pharmacy and the incidence of ADRs has been studied and documented. In this study

majority of the patients (66.7%) belonged to the age group of 60-69 who developed ADRs. This is consistent with the study conducted by Yvonne Koh where a seven fold increase in occurrence of ADRs (21%) in patients aged 60-70 years.¹⁶

The causality of ADRs identified were assessed and documented. All of the ADRs belonged to 'probable' category on WHO scale. Majority (83.3%) of the observed ADRs were 'Mild' in severity. 16.7% was 'Moderate' and none of the ADRs were found to be 'Severe'. All the identified ADRs (100%) were 'Not preventable' and none of them were 'Probably preventable' and 'Definitely preventable'.

Assessment of DRPs by the pharmacist can significantly improve appropriate prescribing in elderly patients with poly pharmacy. In this study the role of the pharmacist has been focused in identification of potential DRPs. About 75% of the recommendations were made to PG medical students followed by physicians (11.2%). This was due to full time availability of PG students in the wards. The nurses were contacted in 8.8% of the DRPs which were concerned with the medication administration to the patients. Very few recommendations (5%) were made to intern students.

The acceptance rate of recommendations was found to be high (97.0%). In 70% of the cases, there was a change in drug therapy. This finding fairly correlates with the study carried out by Ganachari M S⁵ et al where the acceptance rate was 78.3%. Another study conducted by L Bosmaet al¹⁹ also showed similar rate of acceptance (82%) of pharmacists' recommendations. A German study conducted by Langerbake C et al¹⁸ has also shown similar findings where recommendations were made and implemented ranked the highest. In 18% of cases, though the recommendations were accepted, there was no scope for change in drug therapy. These recommendations included counseling the patients regarding the importance of adhering to medications, procuring medicines, suggesting health care professionals to issue prescription for a particular drug. It was also applicable for those DRPs where nurses failed to administer the drug, the ordered dose and administer the drug through correct route. Nine percent (9%) of recommendations suggested were accepted, but change in therapy was not done. This was because the physicians were hesitant to change the prescription immediately because the suggestions were thought to be insignificant. Only 2% of the suggestions were unaccepted.

The overall observation made from this study was that the pharmacist as an integral part of healthcare team and has greater responsibility in minimizing the DRPs in stroke patients. Monitoring the patients for DRPs will decrease the chances of iatrogenic morbidities and contribute for an improved patient care. This will increase the treatment outcomes and overall quality of life of the patients.

CONCLUSION

In our study, drug related problems were identified to occur at a frequency of 1.4 per patient. Majority of the drug related problems were observed in patients in the age group of 60-69 years (25%). Drug-drug interactions (25%) were the most common types of drug related problems identified followed by drug use without indication and adverse drug reactions. Poly pharmacy was found to be a potential risk factor for developing drug related problems. Majority of the recommendations (75%) were made to PG medical students. Although acceptance rate of pharmacist's recommendations was 97%, change in drug therapy was observed only in 70%. Early detection and documentation of drug related problems improve the therapeutic outcomes. Developing and adopting the guidelines regarding the drug administration, dispensing and prescribing would minimize the drug related problems.

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