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Identification And Assessment Of Drug Related Problems In Stroke Patients Admitted To A Tertiary Care Hospital.

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ABSTRACT

To identify the Drug Related Problems (DRPs) in patients with stroke treatment, to study the rate, types, pattern, and clinical significance of DRPs in stroke patients and to investigate the nature and frequency of DRPs along with pharmaceutical interventions to address them in patients with stroke from hospital admission to discharge. A prospective observational study was conducted in a super specialty hospital, Hanamkonda, Telangana, South India for 9 months from December 2014 to August 2015. The patients visiting inpatient department of Neurology were reviewed and patients diagnosed with ischemic and hemorrhagic stroke were enrolled into the study and DRPs in the patients were identified and assessed. 200 patients were enrolled in this study, out of which 117 patients were males and 83 patients were females. 141 patients were with ischemic stroke and 59 were with hemorrhagic stroke. A total of 375 DRPs were identified in 200 patients which included Drug Interactions 35.7% , Indication without drug 24.8% , Adverse Drug reactions 13.8% , Incorrect drug choice 8.2%, Unnecessary long duration 6.1%, Double medication 5.3%, Drugs without indication 3.2% and Contraindications 2.6%. 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.

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INTRODUCTION

The main goal of pharmaceutical care is to optimize the drug therapy, succeed in positive clinical outcomes in reasonable economic expenditures and improve patient's health related quality of life.[1, 2] Availability of latest drug therapies and increased use of medicines increase the risks for patients to induce adverse drug events in the hospitals. Induced adverse events are vital for consideration because they not only prolong the hospital stay but also increase the health care expenditures. [3]

Drugs play a crucial role in the management of illness. Typically use of drugs may result in Drug Related Problems (DRP). [4] A Drug Related Problem (DRP) is outlined as any event or condition involving drug treatment that interferes with the patient achieving best outcome of treatment. [4-8] A Norwegian system for defining and classifying DRPs is graded and consists of six main categories: 1) Drug choice 2) Dosing 3) Adverse Drug Reaction 4) Interaction 5) Drug Use and 6) Alternative. Drug selection which includes extra drug, inessential drug, inappropriate drug selection; Dosing which includes too high dose, too low dose, sub-optimal dosing scheme, sub-optimal formulation; Adverse Drug Reaction (ADR); Interaction; Drug use which includes medication administered by health people, medication administered by the patient; and Other which includes need for/lack of monitoring of effect and toxicity of medication, lack of unclear documentation of the drug chart/prescription and other [4].

Occurrence of DRPs might delay in achieving the required therapeutic goals [3]. Wrong prescription of medicine, increased number of medicines and complex drug regimen might cause DRPs that ends up in ill health, prolonged hospital stay, mortality and cause negative quality of life [9]. DRP might occur at any stage including prescription, dispensing, administration, patient use of medication. [10] Commonest reason behind incidence of DRP is lack of correct follow up and appraisal of treatment chart by health care professionals.

DRPs are often known, resolved, and prevented through pharmaceutical care practices. Pharmacist plays a very important role in identifying actual and potential DRPs, solving actual DRPs and preventing potential DRPs [11]. An actual DRP is an event that has already occurred in a patient, wherever as a possible DRP is an event that's possible to develop if pharmacists don't build any applicable interventions. Studies have shown that majority (50-80%) of DRPs are often prevented by pharmacist interventions. [3]

Although pharmacotherapy will treat diseases and improve the well-being of patients, its advantage is also compromised as a result of drug related problems. Therefore it is necessary to assess drug related problems leading to serious injury or death and analyze whether improvement in the prescribing practices can reduce drug related problems.

Stroke is the commonest cause for death globally and is the leading cause for long term disability in adults, with most of survivors having residual deficits. Incidence of stroke increases with age (especially when age 55), cardiovascular disease and dyslipidemia [12]. Physicians still seek ways to attain higher practical recovery in stroke patients and scale back the devastating impact of stroke on the society [12]. Many studies have shown that elderly age, co-morbidities and poly pharmacy were the main risk factors for DRPs in stroke patients. Therefore, distinguishing and resolving DRPs is a very important priority for health care professionals for improving the therapeutic edges and health connected quality of life in stroke patients. [13]

Pharmacists' participation in patient care (pro-active approach) has evidenced to improve drug compliance with decreasing prescribing errors. This service has reduced health care prices, morbidity and mortality and improved the quality of life. Studies have demonstrated consistent advantages of pharmacist involvement in the management of cardiovascular disease and dyslipidemia, which are thought to be of two major modifiable risk factors in stroke occurrence. Provision of clinical pharmacy services ensures that drugs medical care is optimum, safe, cost-efficient and individualized and helps in reducing drug related issues. [14]

The main objectives of this study were to identify and asses DRPs in stroke patients under treatment along with pharmaceutical interventions to address them in patients with stroke from hospital admission to discharge.

METHODOLOGY

Study was conducted in the department of neurology in a 300 bedded tertiary care hospital from December 2014 to August 2015. The study was approved by Institutional Ethics Committee. Study involved stroke patients (ischemic and hemorrhagic) with or without associated co-morbid conditions of all age groups, of either sex admitted to in-patient wards of neurology department. Patients with risk factors of stroke but not prone to stroke, patients treated on outpatient basis, patients already sensitive to the particular drug were excluded from the study.

A suitable data collection form was designed to collect patient demographics, such as age, sex, and weight, date of admission, date of discharge, reasons for admission and diagnosis, medical and medication history, laboratory parameters, and treatment chart (name of the drug, dose, route, frequency of administration, duration and indication for use), type of drug related problem (DRP) as per the need of the study. Demographic and clinical data was collected for all patients meeting the inclusion criteria. Patients' treatments were monitored on every day and patients were asked about symptoms when necessary. The treatment initiated was analyzed for drug related problems. DRPs observed in the patients were recorded on every day basis. The identified DRPs were recorded and assessed. Physicians were provided information about DRPs and also with suitable strategies to resolve the DRP such as drug interactions, adverse drug reactions and dose adjustment.

RESULTS AND DISCUSSION

The study was conducted in a tertiary care hospital, where total of 436 patients with stroke received medicines like anti platelet agents, Statins, low molecular weight heparin, antihypertensive, oral hypoglycemic agents etc. with an average of 6-7 medicines per patient were reviewed during the study period. Among them 200 patients with at least 1 DRP were identified. The mean age of individuals was 55.30 ± 15.18 yrs (Mean ± S.D). Medication charts of stroke patients with drug related problems were reviewed and an average number of medications received were found to be 9.85 per patient. Out of 200 patients with DRPs, 117 (58.5%) were males and 83 (41.5%) were females. 141 patients (70.5%) were with Ischemic stroke and 59 patients (29.5%) were with Hemorrhagic stroke. Out of 141 Ischemic Stroke patients, 77 patients (54.6%) were males and 64 patients (45.3%) were females. Similarly out of 59 Hemorrhagic Stroke patients, 40 patients (67.7%) were males and 19 patients (32.2%) were females. The most common age group individuals experiencing DRPs were between 61- 70 years (31.5%), followed by 51- 60 years (22.5%). Among 200 patients, 82 (41.0%) patients were found without any co-morbidities and 118 (59.0%) were found to have at least one co-morbidity. Among 118 patients, patients with only one co-morbidity (Hypertension or Diabetes mellitus or Cardiovascular risk) were 83 (70.3%) patients, 32 (27.1%) patients with 2 co-morbidities (Hypertension + Diabetes mellitus or Hypertension + Cardiovascular risk or Diabetes mellitus + Cardiovascular risk) and 3 (2.5%) patients with 3 co-morbidities (Hypertension + Diabetes mellitus + Cardiovascular risk). Demographic characteristics of the stroke patients are presented in Table 1.

Table 1: Demographic Details of Stroke Patients

Patient Characteristics	Number (%) (N=200)		
Gender			
Males	117 (58.5)		
Females	83 (41.5)		
Age (Years)			
1 – 10	02 (1.0)		
11 -20	07 (3.5)		
21-30	06 (3.0)		
31 – 40	14 (7.0)		
41 – 50	42 (21.0)		
51 – 60	45 (22.5)		
61 – 70	63 (31.5)		
71 – 80	18 (9.0)		
81 – 90	03 (1.5)		

Type of stroke		Males Number (%)	Females Number (%)
Ischemic Stroke	141 (70.5)	77 (54.6%)	64 (45.3%)
Hemorrhagic Stroke	59 (29.5)	40 (67.7%)	19 (32.2%)
Number of medication received			
1-5	(13%)		
6-10	(87%)		
Number of Co morbidities			
0	82 (41%)		
1	83 (70.3%)		
2	32 (27.1%)		
3	3 (2.5%)		
Type of co morbidity			
Dyslipidemias	61 (52%)		
Hypertension	28 (24%)		
Diabetes mellitus	15 (13%)		
Cardiovascular problems	14 (12%)		
Length of Hospital stay (in days)			
1-2	4 (2%)		
3-5	67 (33.5%)		
>6	129 (64.5%)		

A total of 375 DRPs were identified in 200 patients during the study period, in which prevalence of DRPs was found to be more in Hemorrhagic cases (2.18%) than in Ischemic cases (1.74%) and the prevalence of DRPs was found to be more in males than in females. The frequency of DRP was 1.8 per patient.

Type of drug related problems identified

Majorly identified drug related problems were drug interactions (35.7%) followed by indication without drug (24.8%), incorrect drug choice (13.8%), side effects (8.26%), unnecessary long duration (6.1%), double medication (5.3%), drug without indication (3.2%) and contraindications (2.6%). Types of DRPS were summarized in table 2, table 3 and figure 1.

Table 2: Distribution of identified Drug related problems based on Gender, Type of stroke and Number of DRP's

	Number of DRPs (%) N=375		
Gender Distribution in DRP's identified patients			
Males	209 (55.7)		
Females	166 (44.5)		
DRP's in different type of stroke patients			
Ischemic Stroke	246 (65.6)		
Hemorrhagic Stroke	129 (34.4)		
Number of DRP's in stroke Patients	Males Number	Females Number	
1	44	25	
2	54	35	
3	15	21	
4	03	02	

Table 3: Distribution of identified Drug related problems based on types

Drug related problem	Number (n)
Drug-Drug interactions	134 (35.7%)
Indication without drug	93 (24.8%)
Adverse Drug Reactions	52 (13.8%)
Incorrect drug choice	31 (8.2%)
Unnecessary long duration	23 (6.1%)
Double medication	20 (5.3%)
Drugs without indication	12 (3.2%)
Contraindications	10 (2.6%)

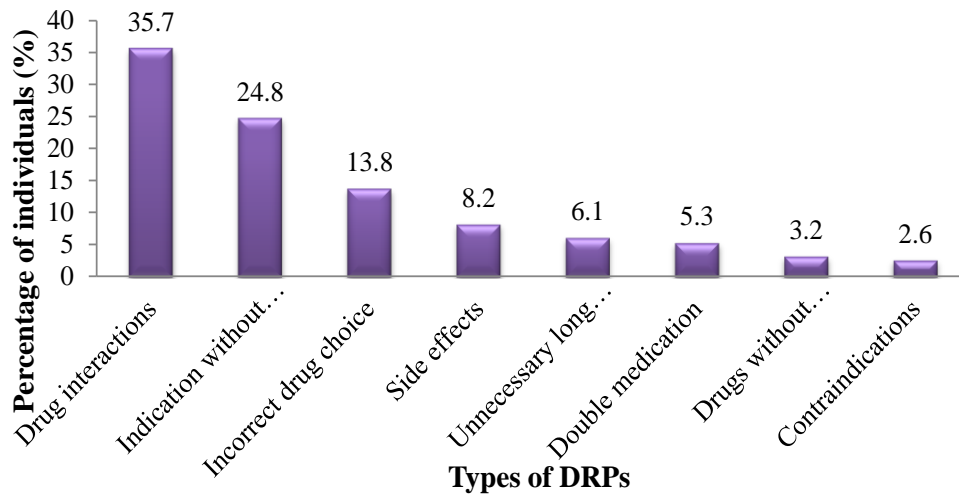


Figure 1: Distribution of identified Drug related problems based on types

Drug Interactions Assessment

Drug interactions were categorized based on severity as major, moderate, and minor. Majority of the observed drug interactions were found 'moderate' (78.3%) in severity, 20.8% was major in severity and 12 (0.7%) were found to be 'mild'. Major interaction was found between nifedipine and dexamethasone in hemorrhagic stroke patients. Moderate interaction was seen between NSAID's and antihypertensives (telmisartan, furosemide, nifedipine, enalapril, metoprolol) which resulted in decreased effectiveness of antihypertensive drugs. Drug interactions involving anticoagulants and Insulin, NSAIDS and Insulin interaction were also moderate resulted in hypoglycemia. Minor drug interactions were seen between aspirin and ranitidine which results in decreased antiplatelet efficacy and ranitidine and bisacodyl interaction resulted in decreased bisacodyl efficacy.

Table 4: Distribution of Drug Interactions based on severity

Severity of Drug Interactions	Number (%)
Major	29 (20.8%)
Moderate	93 (78.3%)
Mild	12 (0.7%)

Adverse Drug Reactions

Adverse drug reactions were assessed by using Naranjo's scale, most of them were found to be probable ADR's (67%) and some were possible ADR's (32.6%). Identified probable reactions were headache with nifedipine, gastric irritation with aspirin, giddiness with citicholine and hypokalemia with insulin. Identified possible reactions were pedal edema with nifidipine.

Suggestions provided

Among the suggestions provided, majority of the suggestions were provided to junior doctors and interns [n=210 (56.0%)] followed by physicians [n= 115 (30.6%)] and nurses [n=35 (9.3%)]. Very few suggestions were provided to senior doctors [n=15 (4.0%)]. The details of suggestions provided are presented in Figure 2.

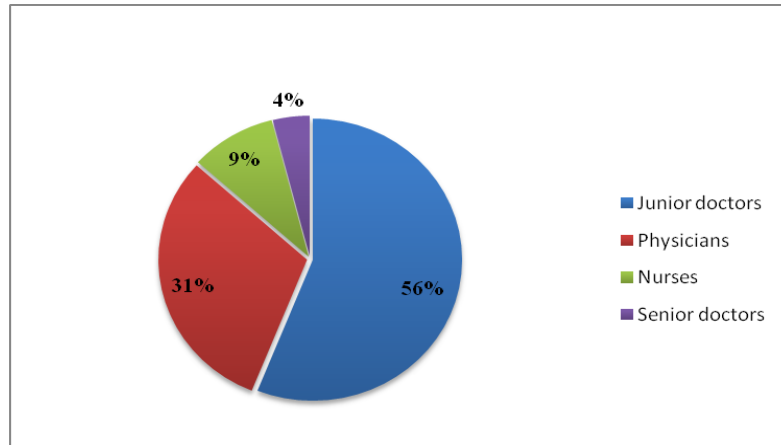


Figure 2: Suggestions Provided

Acceptance rate of DRPs identified

The acceptance rate of DRPs identified was found to be 93.0%. The details of acceptance rate of DRPs are presented in table 5.

Table 5: Acceptance rate of recommendations

Acceptance rate of DRPs identified	Number of DRP's
Accepted and change in drug therapy	220 (59%)
Accepted but change in drug therapy not applicable	87 (23%)
Accepted but not changed the drug therapy	53 (14%)
Not accepted	15 (4%)

DISCUSSION

DRPs are comparatively common in hospitalized patients and may end up in patient morbidity mortality with increase in treatment costs. Increased number of drugs used increases clinical/pharmacological risk factors which contribute to DRPs. Studies have shown that the clinical pharmacy activities decrease drug related issues [15], probability of readmission and total cost of health care. [3]

The present study mainly dealt with the DRPs in prescriptions given for stroke patients. Medicine and neurology departments were chosen for the study because most of the patients with co-morbidities and receiving multiple medicines in single patient were admitted in these departments.

Among 200 stroke patients followed during our study period, 375 DRPs were identified and assessed. Out of 200 patients, 117 (58.5%) were males and 83 (41.5%) were females which is in concordance with the study conducted by Celin AT *et al.* [8] The main reason for this high occurrence in male population is due to male gender predominance in the stroke patients due to various risk factors like smoking, alcoholism and inactive life style and co-morbidities compared to the female population. [5] The total number of DRPs were predominant in males than in females. This observation is also supported with the demographic reports of the study conducted by Ganachari M S *et al* [16], cited a predominance in male gender over female gender. Another study conducted by Madhan Ramesh *et al* [17] has shown similar predominance of males over females.

Predominant DRPs in present study were seen in people of age group 61-70 yrs (31.5%) followed by 51–60 yrs (22.5%) and 41-50 yrs (21.0%). Study conducted by Celin A.T *et al* [8] have also proposed that majority of DRPs were seen in patients in the age group of 60-69 years (25%), which shows similar finding as our study.

Average number of medications received per patient in our study was 9.85. DRPs were seen in patients receiving more than 6 drugs (95%). These findings were in concordance to the study conducted by Vinks *et al* [18] which proposed that DRPs may frequently occur in adults over 65 years of age using six or more drugs concomitantly. This clearly indicates that the main responsible factors for developing DRPs in stroke patients are old age and multiple medicines in single patient.[19] This also indicates that special attention should be done in such group of patients where regular review of drug therapy might help potentially to decrease the drug related problem.[20]

In our study 82 (41.0%) patients were found without any co-morbidity and 59.0% of the patients were observed to have at least single co-morbidity. These study results were supported with the findings of Celin A.T *et al.* [8]

DRPs occurred at a frequency of 1.8 per patient in our study, whereas in study conducted by Celin A.T *et al* [8] it was 1.4 per patient. Predominant DRPs identified in the study were drug interactions (35.7%) followed by indication without drug (24.8%), adverse drug reactions (13.8%) and incorrect drug choice (8.2%). 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%) [20] and also by the study conducted by Ramesh *et al* [8] where drug interactions accounted for 25%.

Drug use without indication is defined as if the indication for a certain prescription was disputable or not evidence-based anymore. [21] 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 [20], 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 of drug interactions (36%) in this study would make this an important area requiring further investigation and the future pharmacist should focus on reviewing patients' medication charts and checking for potential drug interactions regularly. In a German study, conducted by Langerbake C *et al* [22], 'drug use without indication' was found to be second highest which is again comparable with our results. The study conducted by Madhan Ramesh *et al* [17] has also shown a high incidence (18%) of drug use without indication. Probable reasons for these 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.

Adverse drug reactions also create a significant economic burden to the health care system [20]. Out of 200 patients in the study, 52 ADRs (14%) were identified. Identified probable reactions were amlodipine induced constipation, headache with nifedipine, atorvastatin induced myopathy, aspirin induced gastric irritation, citicholine induced giddiness and insulin induced hypoglycemia. Identified possible reactions were pedal edema with nifedipine. Among the risk factors identified, elderly age has been associated with increased risk for developing ADRs. [20]

Our study, results also revealed that the prevalence of DRPs was found to be more in Hemorrhagic patients (2.18) than Ischemic patients (1.74). There were no previous studies conducted showing the results of number of DRPs identified separately in Ischemic and Hemorrhagic stroke, number of DRPs identified separately in males and females and severity of identified Drug-Drug Interactions in respective stroke patients.

Monitoring DRPs in the patient by the pharmacist can considerably improve proper prescribing in elderly patients prescribed with multiple medicines. About 57% of the recommendations were made to junior doctors and interns followed by physicians (30.6%). This was successful because of full time availability of junior doctors in the wards. The nurses were contacted in 9.3% of the DRPs which were concerned with the medication administration to the patients. Very few recommendations (4%) were made to senior doctors.

The acceptance rate of recommendations was found to be high (93.0%). In 60% of the cases, there was a change in drug therapy. This finding correlates with the study carried out by Ganachari M S *et al* [16] where the acceptance rate was 78.3%. Another study conducted by L Bosma *et al* [2] also showed rate of acceptance (82%) of pharmacists' recommendations. A study conducted by Claudia L *et al* [24] has also shown

similar findings where recommendations were made and implemented ranked the highest. In 23% 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. Fourteen percent (14%) of recommendations suggested were accepted, but change in therapy was not done. This was because the physicians were doubtful for prescription change immediately because the suggestions were thought to be insignificant. Unaccepted suggestions were only 4%.

The overall observation made from this study was that the pharmacist as an integral part of healthcare team has greater responsibility in minimizing the DRPs in stroke patients. Monitoring the patients for DRPs will decrease the chances of drug induced 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 a total of 375 DRPs were identified in 200 patients during the study period, in which prevalence of DRPs was found to be more males than in females. The frequency of DRP was 1.8 per patient. Predominant DRPs identified in the study were drug interactions (35.7%) followed by indication without drug (24.8%), adverse drug reactions (13.8%) and incorrect drug choice (8.2%).

Potential drug interactions, co-morbidities and polypharmacy were the most common factors found in this study. Majority of the recommendations (57%) were made to junior doctors and interns. Although acceptance rate of pharmacist's recommendations was 93%, change in drug therapy was observed only in 60%. Early identification and prevention of DRPs and rational use of drugs in stroke are necessary to prevent complications and unnecessary hospitalization, high cost of treatment and deaths among stroke patients. Developing and adopting the guidelines regarding the drug administration, dispensing and prescribing would minimize the drug related problems.

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