A Clinical Study On Assessment Of Drug Related Problems In Geriatric Patients At Tertiary Care Hospital

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Abstract
The geriatric population is at high risk of drug related problems (DRPs) due to the age-related pharmacokinetic and pharmacodynamic changes. Furthermore, a higher incidence of drug related problems could result from age associated increased prevalence of multiple chronic diseases, which causes the use of complex therapeutic regimens. Drug-related problem (DRP) can be defined as: 'an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes'. According to this point of view, a potential problem is a circumstance that may result in drug-related morbidity or fatality if no exploit is carried out. To assess Drug related problems in geriatric Patients and its possible contributing factors. A totally 300 patients were participated in this study, among the subjects reveals that 170 were male while 130 were female. 38.3% out of total subjects were higher between 65-70 years of age, In the study population of geriatrics among males was 56.6% and among females was 43.3%. More geriatrics was observed among male gender. The mean age of males were 56.6±53.0 and females were 43.3±41.2.A total of 541 DRPs were identified in all 300 study subjects, having a DRP frequency of 2.36 ± 2.01 per patient and categories as related to; drug without indication 4.06%, indication without drug 4.43%, drug not appropriate for therapy 2.77%, supratherapeutic dose 0.55%, additive toxicity 0.88%, therapeutic duplication 2.21%, adverse drug reactions 8.13%, drug–drug interaction 22.55% and PCNE assessment of potential inappropriate medications in elderly prescribing 51.08%. Of the total 541 indirect intervention recommended by clinical pharmacist, 162 were implemented, 324 were apprehended and acknowledged and 55 were unknown for their outcomes. Our study findings concluded that provide insight into the type of pharmaceutical care service required. Pharmacists and physicians could collaborate to develop drug use guidelines and policies in developing a safer healthcare system; this study advocates for the possibility of a collaborative and joint effort.

Key words: Drug related Problems, geriatrics and pharmaceutical care

INTRODUCTION

The geriatric population is at high risk of drug related problems (DRPs) due to the age-related pharmacokinetic and pharmacodynamic changes. Furthermore, a higher incidence of drug related problems could result from age associated increased prevalence of multiple chronic diseases, which causes the use of complex therapeutic regimens. Related to this, population aging has resulted in an increased prevalence of chronic diseases and thus rise in hospitalizations and healthcare costs of older adults[1].

The world geriatric population was found to be 21% as per 1991 census reports. In India, the geriatric population was found to be 57 million. With the advancement in medical technology and important social, financial, health care planning implications, the geriatric population for 2050 illustrate about 324 million i.e.33% of the world population. In India 7.7% of its populations are more than 60 years old, and has acquired the label of "an aging nation" with in which 75% of elderly persons were living in rural areas.

Drug-related problem (DRP) can be defined as: 'an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes'. According to this point of view, a potential problem is a circumstance that may result in drug-related morbidity or fatality if no exploit is carried out; an actual problem is always associated with signs and symptoms[2]. Actual problem should be differentiated from potential problem and drug related problem is used to specify a drug related incident bendable problem on the health-end effect of the pharmacotherapy. The drug-related problem will not exist if there is no possible persuade[3].

Drug-related problems mainly comprise of medication errors (error that occurs during the process of prescribing, dispensing, or administering a drug, whether there are adverse consequences or not) and adverse drug reactions (any response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function. The inter individual

variability among elderly people in health, disability, age related changes, poly morbidity and poly pharmacy associated along with this makes generalisation of prescribing recommendations often difficult in these patients[4].
Drug-related problems are the common and frequent in hospitalized patients where multiple changes in patient's medication regimens occurs as result of multiple comorbidities and lack of continuity of care[5]. Problems associated with drug use are many and includes inappropriate prescribing of medicines, mismatch between prescribed and actual regimens, decreased medication adherence, drug interactions, inappropriate use of drugs, patients monitoring and inadequate surveillance for adverse drug reactio[6] etc.

METHODOLOGY

A prospective observational study was conducted in jayabharath hospital Nellore, for a period of 3 years. The study involved data collection of patients by conducting regular ward rounds and identification of patients to be included in the study. Demographic characteristics such as age, gender and clinical characteristics such as clinical diagnosis, duration of hospital stay, presence of associated comorbidities, drug therapy profile, and concurrent medications were collected on designed data format, clinical and drug therapy review were performed on day to day basis to identify and report any occurrence of DRP's by means of a checklist tool specifically developed to identify commonly occurring DRP's using the PCNE classification scheme[7] for use by clinical pharmacist. Using the checklist relevant information was reviewed by clinical pharmacist to identify and categorized DRP's. The identified DRPs were assessed for its possible cause and further intervened indirectly in consultation with the treating physician for possible recommendation to resolve them. Microsoft office 2007 excel worksheet was used to compute and report all the data collected and extracted in this study.

The study involved data collection of patients by conducting regular ward rounds and identification of patients to be included in the study. The drug related problems like medication errors, adverse drug reactions and drug interactions will be monitored and the medication related problem documentation form was used to document the DRP provided by the clinical pharmacist. All these details were collected from the patient by interviewing each patient and through checking the medical records.
Based on inclusion and Exclusion criteria patients were included in the study.

Inclusion Criteria:

- Patients of either sex of 60 years and above.
- Patient who are willing to give consent.

Exclusion Criteria:

- Patients not ready to respond to the query.
- Unconscious patients. (e.g. continuous coma state).

RESULTS

A totally 300 patients were participated in this study, among the subjects reveals that 170 were male while 130 were female. 38.3% out of total subjects were higher between 65-70 years of age, In the study population of geriatrics among males was 56.6% and among females was 43.3%. More geriatrics was observed among male gender. The mean age of males were 56.6±53.0 and females were 43.3±41.2 showed in (Table No 1) presence of associated comorbidities observed in 205 (68.3%) patients The average duration of hospitalization was 5 ± 2.3 showed in (Table No 2) days. Polypharmacy was common, More number of patients (30.6%) are using OTC drugs 1-5 range and rest of them are using in the range of 6-10 (21.6%) and >11 (7.3%) drugs respectively.

A total of 541 DRPs were identified in all 300 study subjects, having a DRP frequency of 2.36 ± 2.01 per patient and categories as related to; drug without indication [DWI] 4.06%, indication without drug 4.43%, drug not appropriate for therapy 2.77%, supratherapeutic dose 0.55%, additive toxicity 0.88%, therapeutic duplication 2.21%, adverse drug reactions (ADR) 8.13%, drug–drug interaction 22.55% and PCNE assessment of potential inappropriate medications in elderly prescribing 51.08% (Table 3).

Of the total 541 indirect intervention recommended by clinical pharmacist, 162 were implemented, 324 were apprehended and acknowledged and 55 were unknown for their outcomes (Table 4).

DISCUSSION

A total of 541 DRPs were identified in all 300 study subjects, having a DRP frequency of 2.36 ± 2.01 per patient and categories as related to; drug without indication [DWI] 4.06%, indication without drug 4.43%, drug not appropriate for therapy 2.77%, supratherapeutic dose 0.55%, additive toxicity 0.88%, therapeutic duplication 2.21%, adverse drug reactions (ADR) 8.13%, drug–drug interaction 22.55% and PCNE assessment of potential inappropriate medications in elderly prescribing 51.08%. (Table No.3)
The most common complication was of hypoglycemia 72(24%) similar to the study reported by Huang ES et al., (18), which reported most common complications of cardiovascular events followed by DM(11.3%), Respiratory system

disorder (7.6%), Chronic kidney disease (7%). Coronary artery disease (6.6%) and Gastrointestinal disorder (5%%). The study observed polypharmacy (94.31%) and increased Length of hospital stay of the patients with 1to 5 days 50.6% in study population as potential circumstances which are dramatic, since plethora of diabetic disease state (comorbidity, complications, and complexity of treatment) together with vulnerable elderly characteristics (impaired pharmacokinetic, pharmacodynamic and metabolic functioning) and clinical situations arising out of negative prognosis, necessitate unwavering and multiple medication management, posing high risk for DRP's occurrence[8].

DRUG RELATED PROBLEM

Drug without Indication

Drug without indication explains about a medication being prescribed by thehealth care professional to the patient, but the patient lacks the definite indication forthat medication usage. The study observed 22(6.17%) drugs whose indications were not clearly or appropriately established for its usage. The possibility of such drugs being prescribed may have varied reasons ranging from lacking specific clinical condition, unclear diagnosis, peer practice lacking substantial evidence and delinquency in prescribing.

Indication without Drug

Indication without drug expands the presence of a specific clinical conditionwhich requires a medication therapy, but the physician or any other healthcare prescriber fail to order medication for that specific condition. The study observed 24(4.06%) indication for which drugs were not prescribed. The study observed an incidence of IWD occurring at every 3.96 patients. The study observed IWD comprises 3.96 as an average of DRP per patient as similar to a studyreported by Farrell, Szeto & Shamji (2011), where drug without indication comprises of 2.75 as an average of DRP per patient and 1.75 for indication without drug.

Drugs not appropriate for therapy

It is an inappropriate one, in terms of selection or choosing a drug, in order to treat a specific indication. The study observed 2.77% of total DRP as drugs not appropriate for therapy. These drugs
were ceftriaxone 04(26.6%), Metoprolol 03(20%), ofloxacin + ornidazole 2 (13.3%), Tramadol 2 (13.3%), Aspirin+Clopidogrel 2 (13.3%), Glimepride01(6.6%) and Mefloquine 01(6.6%), The observed data was not complained with established literature evidence for given clinical situation for its use, but for a given clinical situation the approach in using a drug therapy usually weighed on risk ratio, sometime drugs were prescribed based on evidence base medicine practice, the justification probably attributes to itsoff labelled therapeutic use and compatibility issues, and to a certain extent its reported effectiveness at local ethnic or geographical level.

Therapeutic Duplication

The study observed 07(2.52%) therapeutic duplication of medications in study population, contributing to total DRP's reported.Around 12 cases of drug duplication or therapeutic duplication observed among study population related the following drug categories Amlodipine (16.6%), Pantaprazole(16.6%), Ondansetron (8.3%) Midazolam(8.3%) Furosemide(8.3%) Rabeprazole(8.3%) Metformin(8.3%) Spironolactone(8.3%) Atorvastatin(8.3%) and amoxicillin(8.3%)were respectively. Over prescribing, confused schedule, deficient patient case record documentation, available of multiple mediciation brands for a single molecule and reduced apprehension to acknowledge different brands having same active ingredient, indecipherable prescription by prescriber, frequent changing orders of drug and drug dosage forms, communication gap between health care team, similar look alike or similar pronouncing styles or spell alike drugs , monotherapy and combo therapy of similar medications etc were some reported reasons for drug duplication episodes.

EFFICACY RELATED DRPs

Supra therapeutic Dose

It indicates prescribing high level of doses for the treatment for an indication, then the required, supra and sub therapeutic dose contributing[9]. The efficacy DRPs were categorized as administration of drug dosage more or in excess than therapeutic prescribing standard as referred to supratherapeutic dose or lesser than therapeutic prescribing standard referred to as sub therapeutic dose or under prescribing of drug dosage, either of which may be a reason for drug therapy effectiveness. The study observed more than recommended doses in study patients with possible assessment related to negligence during prescribing, inappropriate dosageform regimens resulting in potential DRPs.

Additive toxicity

Additive toxicity, It is a toxic effect caused by a drug when it is prescribed in a higher dose and it is required serum level of a drug treatment above therapeutic window and at a concentration which haspotential to precipitate drug toxicity. The study observed (0.88%) of total DRP as episode of additive toxicity shown Ramipril + Amlodipine and assessment reveals due to the evidence based therapy where the patient condition demands the situation for a higher dose. An episode of additive toxicity observed in the study due of higher dosing, such prescribing are usually

observed during a clinical condition which demands an increase in dose to ascertain clinical effectiveness of drug therapy by careful evaluation of risk and benefitratio of increasing dosage.

Adverse Drug Reactions

The study observed 8.13% episodes of ADRs, the commonest ADR observed was metallic taste, altered sensorium, and nausea etc. The impact of ADR certainly poses a significant risk of treatment outcome in elderly, the financial burden on health care system, besides undesirable consequences for the patients[10]. The ADR reported, were mild to moderate and self-limiting in nature. Recommendations for all the suspected ADRs were recognized.

Drug drug interactions

The study reported 122 drug interactions 22.55%. Of which, Major interactions 16 (12.75%) and Moderate interactions 130(87.24%) which implies 15.44% of the subjects had reported with at least one major drug interactions and everyone had been subjected to one or more moderate drug interactions, similar to thestudy carried out by Ibrahim, Kang, Dansky[11], where 38.8% of the study samplecould potentially be exposed to minimum one rigorous drug drug interaction and all most all the study subject (92.8%) were at risk of exposure to modest drug drug interactions. The study reveals possible reasons of inappropriate timing of administration or dosing intervals, multiple medications or polypharmacy, multiple diagnoses or associated co-morbidity, drug characteristics of potential incompatibilityand lack of appropriate information and knowledge about the drug pharmacokineticsetc

Assessment of PCNE

Potentially inappropriate medication use in elderly people was assessed by PCNE which comprises a list of medications that pose potential risks outweighing potential benefits whenever subjected for its use in elderly.

The pharmaceutical care network Europe (PCNE) has classified drug related problemsinto different categories like problems, causes, interventions, outcome and the currentversion approved is V5. According to this there are four primary classifications forproblems like P1 to P4, causes are divided into 8 primary classes from C1 to C8,Interventions are of 5 types from I0 to I4, and Outcomes are of 4 types from O0 to O3.These are again subdivided into different types, problems are again subdivided to 9 types, causes have 37 subtypes, and interventions have 17 subdivision and outcome seven[12].

A total of 300 patients were screened for DRPs. Among them, 80 patients have at least one DRP. A total of 92 DRPs were identified. As per PCNE classification, the problems the DRPs were categorized. The problem of the Effect of drug treatment not optimal was found to be the highest which accounted for (code P1.2, n=34) 36.95% of DRPs followed by that of the suboptimal effect of Further clarification necessary with (code P4.2, n=26) 28.26%. The major DRP was found to be in this study was problem with treatment effectiveness 125(39.5%) followed by adverse drug reaction 56(60.08%), Treatment cost 10(10.86%) and other problems 26(28.26%).(Table No:5)

Causes for each DRPs were also found with the aid of PCNE criteria. Causality assessment revealed that improper drug selection was the major cause of DRPs 63 (68.47%) followed by dose selection 15(16.30%), Treatment duration 2(2.17%), Drug use process 2(2.17%), Logistics 10 (10.86%)and Patient 1(1.8%) respectively. Among different causes of DRPs that were identified during the study, the problems caused due to the requirement of the Inappropriate drug were found to be the highest with (C1.1)19.56% which is followed by problems caused due Indication for drug treatment not noticed with (code C1.5, N=12) 13.04%.(Table No:6)

The above results showed that Interventions were also made in regard to each to DRP. Interventions were put forward at various levels, namely patient level, drug level and others. Intervention put forward at prescriber level were higher 79(69.2%). Followed by patient level 11(9.6%) and drug level 17 (15%)(Table No:7).

There are 5 types of interventions done to reduce or minimize DRPs. In some case no interventions will be required, since there is only chances of occurrences of DRPs and therefore not necessary to do any intervention.

Final outcomes of the proposed intervention were also evaluated and it was found to that 44.31% of drug related problems was completely solved and 18.18% of drug related problems was partially solved and not solved 13.63%(Table No:8).

Pharmacists' interventions to resolve the DRPs

Pharmacist Intervention for DRP and Outcomes All the identified 364 DRPs were subjected for the scope of pharmacist intervention (indirect). A majority of the recommendations made by clinical pharmacists were accepted (89.7%), of which 29.9% were implemented, 59.8% were apprehended and acknowledged, and 10.1% were unknown for their outcomes(Table No:4) A few suggested interventions were subjected for supplementary evidence to implement the change.

The study presented an opportunity to the clinical pharmacists to optimize patient care by identifying, resolving and preventing drugrelated problems in the study population and a challenge to clinicians to carefully evaluate the medication profile, to provide the safest, most efficacious and simplest medication regimen possible meeting an

individual patient requirement[13]. The study could not assess the impact of identified DRPs on disease morbidity due incomplete patient record[14].

CONCLUSION

The findings of the current study was concluded that emphasize the significance of reporting DRP to patients in order to provide improved health care. The need for medication review is useful at admission and at discharge to minimize DRPs Strategies to address problems related to dose adjustment are required during hospital stay, together with ongoing clinical pharmacist review. Our findings provide insight into the type of pharmaceutical care service required.Pharmacists and physicians could collaborate to develop drug use guidelines and policies in developing a safer healthcare system; this study advocates for the possibility of a collaborative and joint effort.

Table No:1 age wise gender distribution

S. No	Age	Male	Female	Total	Percentage
1	65-70	62	53	115	38.3
2	71-75	36	31	67	22.3
3	76-80	37	24	61	20.3
4	81-85	25	13	38	12.6
5	86-90	10	9	19	6.3
Total		170	130	300	
Mean ±SD	56.6±53.0	43.3±41.2			

Table No. 2: Length of stay in hospital among study subjects

Length of hospital stay	No. of patients	Percentage
1-5	178	50.6
6-10	101	38.7
>10	21	10.6
Total	300	-

Table No:3 Categorization and distribution of DRPs

s.no	DRP Categories	Sub categories	Frequency	Percentage (%)
1	Indication Related	Drug Without Indication	22	4.06
		Indication Without Drug	24	4.43
		Drug Not Appropriate	15	2.77
		Therapeutic Duplication	12	2.21
2	Efficacy Related	Supra/sub therapeutic dose	03	0.55
3	Safety Related	Additive toxicity	01	0.18
		Suspected ADR	44	8.13
		Drug –Drug Interaction	122	22.55
4	PCNE classification Assessment	For geriatrics	298	55.08
	Total DRPs		**541**	**100**

Table No:4 DRP's and Outcomes of Pharmacist Indirect Interventions DRP Categories

Interventions DRP Categories	No. of DRPs	Outcomes of Interventions		
		Implemented	Apprehended	Not known
Drug Without Indication	22	8	11	3
Indication Without Drug	24	9	10	5
Drug Not Appropriate	15	7	5	3
Therapeutic Duplication	12	5	3	4
Supra and sub therapeutic dose	03	1	1	01
Additive toxicity	01	1	0	0
Suspected ADR	44	24	11	9
Drug –Drug Interaction	122	52	61	9
PCNE Assessment	298	55	222	21
Total	541	162	324	55

Table No: 5 PCNE Classification of drug-related problems

Code		Drug related problem	Total number	Percentage
P1		Treatment effectiveness	56	60.08
	P1.1	effect of drug treatment/therapy failure	0	0
	P1.2	Effect of drug treatment not optimal	34	36.95
	P1.3	Wrong effect of drug treatment	12	13.04
	P1.4	Untreated indication	20	21.73
P2		Adverse reactions	6	6.52
	P2.1	Adverse drug event (nonallergic)	6	6.52
	P2.2	Adverse drug event (allergic)	0	0
	P2.3	Toxic adverse-drug-event	0	0
P3		Treatment costs	10	10.86
	P3.1	Drug treatment more costly than necessary	0	0
	P3.2	Unnecessary drug-treatment	10	10.86
P4		Others	26	28.26
	P4.1	Patient dissatisfied with therapy despite optimal clinical and economic treatment	0	0
	P4.2	Further clarification necessary	26	28.26
		Total	92	-

Table No:6 PCNE Causes of drug-related problems

Code		Drug related problem	Total number	Percentage
C1		Drug selection	63	68.47
	C1.1	Inappropriate drug (including contraindicated)	18	19.56
	C1.2	No indication for drug	0	0
	C1.3	Inappropriate combination of drugs, or drugs and food	10	10.86
	C1.4	Inappropriate duplication of therapeutic group or active ingredient	9	9.78
	C1.5	Indication for drug treatment not noticed	12	13.04
	C1.6	Too many drugs prescribed for indication	2	2.17
	C1.7	More cost-effective drug available	0	0
	C1.8	Synergistic/preventive drug required and not given	10	10.86
	C1.9	New indication for drug treatment presented	2	1.58
C2		Drug form	0	0
	C2.1	Inappropriate drug form	0	0
C3		Dose selection	15	16.30
	C3.1	Drug dose too low	10	10.86
	C3.2	Drug dose too high	5	5.43
	C3.3	Dosage regimen not frequent enough	0	0
	C3.4	Dosage regimen too frequent	0	0
	C3.5	No therapeutic drug monitoring	0	0
	C3.6	Pharmacokinetic problem requiring dose	0	0
	C3.7	Deterioration/improvement of disease state	0	0
C4		Treatment duration	2	2.17
	C4.1	Duration of treatment too short	2	2.17
	C4.2	Duration of treatment too long	0	0
C5		Drug use process	2	2.17
	C5.1	Inappropriate timing of administration and/or dosing intervals	2	2.17
	C5.2	Drug underused/under administered (deliberately)	0	0
	C5.3	Drug overused/over administered (deliberately)	0	0
C6		Logistics	10	10.86
	C6.1	Prescribed drug not available	0	0
	C6.2	Prescribing error (necessary information missing)	10	10.86
C7		Patient	1	1.08
	C7.1	Patient forgets to use/take drug	1	1.08
	C7.2	Patient uses unnecessary drug	0	0
	C7.3	Patient takes food that interacts	0	0
	C7.4	Patient stored drug inappropriately	0	0
C8		Other	0	0

	C8.1	Other cause; specify	0	0
	C8.2	No obvious cause	0	0
		Total	92	

Table No:7 Intervention as per PCNE

Primary Domain	Code V6.2	Intervention	Total No.	%
No intervention Needed	10.0	No Intervention	6	5.26
At Prescriber Level	11.1	Prescriber informed Only	15	13.15
	11.2	Prescribed asked for information	14	12.28
	11.3	Intervention Proposed, approved by Prescriber	17	14.91
	11.4	Intervention Proposed, not approved by Prescriber	12	10.52
	11.5	Intervention proposed, outcome unknown	21	18.42
At Patient/Career Level	12.1	Patient(medication) Counselling	1	0.87
	12.2	Written Information provided only	1	0.87
	12.3	Patient referred to prescriber	3	2.63
	12.4	Spoken to family member/caregiver	6	5.26
At Drug Level	13.1	Drug changed to	4	3.50
	13.2	Dosage changed to	3	2.63
	13.3	Formulation changed to	0	0
	13.4	Instructions for use changed to	6	5.26
	13.5	Drug Stopped	1	0.87
	13.6	New Drug started	3	2.63
Other Intervention or activity	14.1	Other Intervention(Specify)	1	0.87
	14.2	Side effect reported to authorities	0	0

Table No.8 Outcome of Intervention

Primary Domain	Code V6.2	Outcome of Intervention	Total No.	%
Not known	O0.0	Outcome Intervention not known	21	23.86
Solved	O1.0	Problem totally solved	39	44.31
Partially Solved	O2.0	Problem Partially solved	16	18.18
Not Solved	O3.1	Problem not solved, lack of cooperation of patient	12	13.63
	O3.2	Problem not solved, lack of cooperation of	0	0
	O3.3	Problem not solved, intervention not effective	0	0
	O3.4	No need or Possibility to solve problem	0	0

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