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A Study to Identify and Assess Drug-Drug Interactions among Geriatric Patients - A Community Based Study

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ABSTRACT

Drug interaction occurs due to concomitant administration of drugs with food, beverage, supplement or another drug, which can alter the pharmacokinetics of another drug. Drug-drug interactions occur when two or more drugs react with each other, resulting in drug toxicity and increased adverse events. As age advances, more diseases develop resulting in the use of more medications, hence geriatrics are more susceptible to drug–drug interactions because of their increased age and altered physiological functions. The risk for drug interactions and drug-related problems increases along with multiple medications. Periodic evaluation of the patient's drug regimen is essential to minimize polytherapy.

In the present study, patients above 60 years of age with multiple chronic medications for various indicative ailments were included for identifying and assessing drug-drug interactions. On analyzing the data, total of 150 prescriptions exhibited polypharmacy, in which 138 prescriptions were prescribed with less than or equal to 10 drugs and 12 prescriptions with more than 10 drugs. Understanding the severity of drug-drug interactions out of 150 prescriptions, there were 196 interactions comprising 44 (22.7%) major ones; 133 (68%) moderate and 78 (40%) minor interactions. Potentially inappropriate medications were identified as per American Society of Beer's geriatric guidelines 2019 which can be dangerous as there is an increased chances of drug toxicity and adverse events. This study suggests that pharmacist interventions can play a major role in identifying and assessing drug-drug interactions in geriatric patients.

Keywords: Drug-interactions, Polypharmacy, Geriatrics, Beer's criteria, Pharmacokinetics

INTRODUCTION

Polypharmacy is defined as the administration of five or more drugs in a prescription. Drug prescription in elderly is a serious challenge as there is an increased possibility of drug interactions resulting in toxicity, treatment failure or loss of drug effect [1,2]. Polypharmacy could arise among regular use medications as inappropriate addition of multiple medications due to lack of indication, efficacy, therapeutic duplicity, prolonged use of irresponsible medication or irrational overdosing [2,3]. Polypharmacy as an unchecked phenomenon nowadays cause various troubles, issues and complications such as drug interactions, adverse eventualities, heightened medical costs and very feeble medication adherence [4,5]. Medications of the order of five or even more [6] quite often spawned more adverse drug reactions and decreasing patient adherence [8]. Furthermore, immoderate indulgence in excessive polypharmacy and its abuse (ten or higher medication) have many a time witnessed death [10].

BEER'S CRITERIA

The beer's criteria were first developed in 1991 to asses inappropriate prescribing and ADEs, in particular to identify medications or medication classes that should be avoided in older adults. The 2019 American geriatric society beers criteria contain six tables: PIMs in older

adults, drug-disease or drug syndrome interactions that may exacerbates the disease or syndrome, drugs to be used with caution in older adults, medications that should be avoided or have their dosage reduced with varying levels of kidney function in older adults, and drugs with strong anticholinergic properties.

Beers criteria is the most widely-cited criteria used to assess inappropriate drug prescription [11] as a list of medications considered inappropriate for older patients, either because of ineffectiveness or high risk for adverse events (AE).

The primary aim of the study was to sensibly detect the possible drug interactions, optimizing the prescription of appropriate polypharmacy for older patient pool, the produced knowledge results would prove helpful to optimize any future perspectives.

MATERIALS AND METHODS

STUDY SITE: A Prospective observational study was carried out in Geriatric Community resident of Mangalore, Karnataka, India.

STUDY DESIGN: Community based Prospective and Observational Study. The study was conducted for a duration of 6 months from September 2019 to February 2020.

ETHICAL CLEARANCE: The study protocol was approved by the Institutional Ethics Committee (IEC) of Srinivas Institute of Medical Sciences and Research Centre, Mukka, Mangalore. (Reference number 2019/10/28/5)

STUDY CRITERIA:

- **INCLUSION CRITERIA**

1. All subjects of both gender above 60 years of age.
2. Subjects prescribed with five or more drugs.
3. Subjects who are willing to participate in the study.

- EXCLUSION CRITERIA

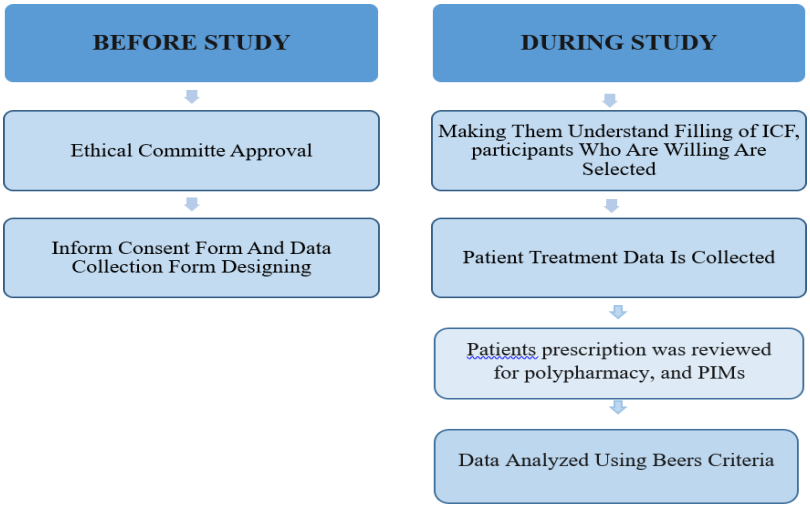
1. Patients having psychiatric disorders.
2. Subjects prescribed with less than five drugs.

SOURCE OF DATA: Data's were taken from the subject's medical files which includes past medical history, current medications and also by direct face-face interview using questionnaire.

STUDY METHOD: Medical records of the subjects has been collected, and were appropriately questioned them using the data collection form which included the demographic details, drug listing under medication regime, questionnaire responses and pharmacist interventions. The possible drug interactions in the prescriptions were noted, recorded, tabulated and appraised.

DATA ANALYSIS: Data were collected and analyzed using the Microsoft Excel and the following results were represented graphically. Inappropriateness of medications were analyzed using Beer's Criteria.

OPERATIONAL MODALITY:



RESULTS

The present study included 150 subjects who met inclusion criteria age category between 60-94 years were the selected for sampling pool and they had undergone screening with interviewer-administered verbal questionnaire (as principal data collection tool). The registry showed 11(13.92%) male subjects in 60-65 age groups; 51(64.55%) male subjects in 66-75 age groups and 17 (21.55%) male subjects in more than 75 age groups, whereas 12 (16.90%) female subjects in 60-65 age groups; 39 (54.92%) female subjects in 66-75 age groups; and 20 (28.15%) female subjects in more than 75 age groups were found.

TABLE 1: Depicting the age group results in 150 subjects

Gender	Age group	Number of subjects	% of males or females	% of total sampling population
MALE		79		52.60
	60-65	11	13.92	
	66-75	51	64.55	
	>75	17	21.5	
FEMALE		71		47.30
	60-65	12	16.90	
	66-75	39	54.92	
	>75	20	28.15	

Analyzing the incidence of polypharmacy among cases studied, the indicative threshold index of overload was marked above 10 drugs (Fig.1). Among the 150 patients, initial categorization was upon number of drugs profile prescribed with 5 to 10 was 138 (92%) and more than 10 was 12 (8%). The 10-count drug application was a median point, where severity of drugs or drug classes or frequency employed was willfully assumed immaterial in the polypharmacy patient group studied.

TABLE 2: Demographic details and characteristics of patients

Details	Characteristics	Number
GENDER	Male Female	79 (52.7%) 71 (47.3%)
AGE	Chronological age Early elderly Late elderly	23(15.33%) 90(60%) 37(24.67%)
NUMBER OF DRUGS PRESCRIBED	≤10 >10	138 (92%) 12(8%)

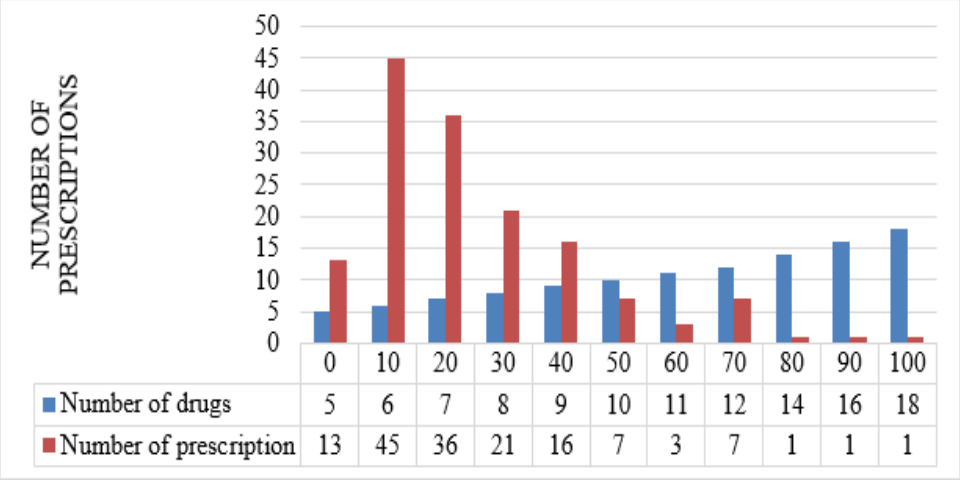


Figure 1. Depicting incidence of polypharmacy.

A total of 150 subject's prescriptions were collected and were found to have drug interactions. Out of 150 prescriptions total number of interactions was found to be 196 (Fig.1). The drug interactions were classified as major, moderate, minor and no interactions. Out of 196 interactions 44 (22.7%) major interactions, 133 (68%) moderate interactions and 78 (40%) minor interactions were found (Fig.2). The most commonly observed major drug interactions among our study population were

Clopidogrel+Aspirin, Aspirin +Atorvastatin, Clopidogrel + Proton pump inhibitors, Risperidone + Quetiapine, Glimepiride and Warfarin (Table.3).

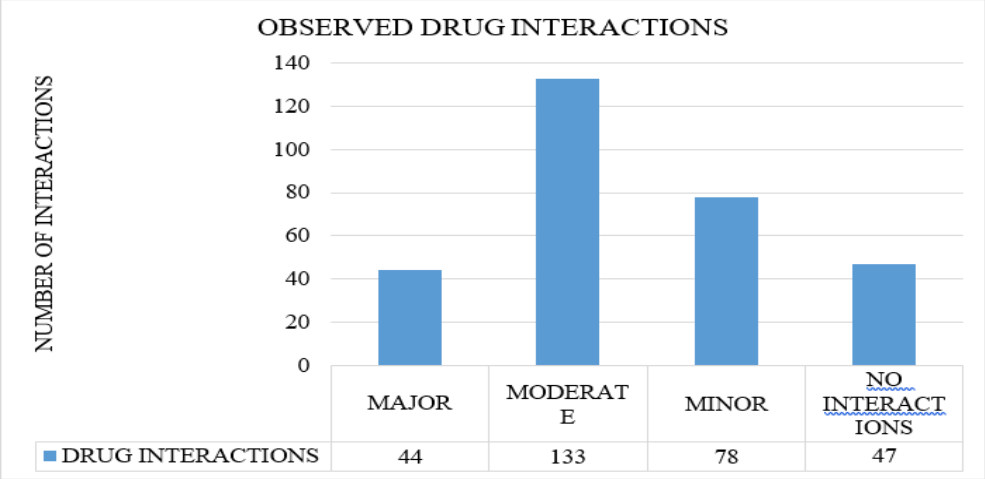


Figure 2: Number of drug interactions found in 150 patients

Table 1. Visible Indication of Co-Drug Physiological Interactions Found in 12 Polypharmacy Cases (>10 drugs/case)

POLYPHARMACY CASES WITH >10 DRUGS	POLYMEDICATION DRUGS	ANTAGONISTIC DRUG COMBINATIONS	CLINICAL INTERVENTIONS
CASE 1	Propranolol with Levodopa/Carbidopa Telmisartan and Risperidone	Both levodopa and propranolol can increase the risk of hypotension Lower initial doses or slower dose titration of risperidone; increased risk of stroke.	Substituting ranitidine for pantoprazole inhibits CYP3A4, one of the isozymes responsible for risperidone metabolism
CASE 2	Risperidone with anxiolytics, sedatives and hypnotics	Clonazepam and quetiapine both increase sedation	Quetiapine increases effects of trihexyphenidyl by pharmacodynamics synergism primary CNS effects of risperidone
CASE 3	Atorvastatin, amlodipine and anti- platelets	Torsemide and amlodipine may cause deterioration in renal function, including renal failure	Clopidogrel increases levels of torsemide by decreasing metabolism; aspirin increases and torsemide decreases serum potassium
CASE 4	Xanthines and calcium channel blockers	Nifedipine + theophylline affects hepatic/intestinal enzyme CTP3A4 metabolism	Diltiazem and nifedipine both increase anti- hypertensive channel blocking
CASE 5	Anti-Parkinson agents Dopamine precursors	Aspirin, sodium bicarbonate decreases effects of nebivolol by pharmacodynamics antagonism	Nebivolol and aspirin/citric acid/sodium bicarbonate both increases serum potassium
CASE 6	α-agonist hypotensive agent; serotonin/5HT3 antagonist; dihydropyridine; calcium channel blockers	Ketoconazole (CYP3A4 inhibitor) with ondansetron (CYP3A4 substrate) elevates ondansetron plasma concentration and QT prolongation	ECG monitoring warranted
CASE 7	CCB's with TCA	Verapamil increases effects of insulin	Cardiac dysrhythmic effects. Amitriptyline and monoxidine both increase sedation.
CASE 8	ARB's and Insulin	Valsartan increases effects of insulin	Concomitant use of insulin and angiotensin receptor blocker (ARB's) require insulin adjustment continual glucose monitoring
CASE 9	ARB's and NSAIDS with anti-platelet (Blood Thinners)	Telmisartan, ibuprofen mat result in geriatric renal function deterioration; ibuprofen decreases temisartan by antagonism; clopidogrel and NSAIDS inhibit platelet aggregation	Deflazacort decreases aspirin increases renal clearance. Aspirin and ibuprofen elevate serum potassium.
CASE 10	PDE5 enzyme inhibitors with hypnotics and narcotics	Chlorpheniramine and tramadol both increases sedation	Calcium carbonate + aspirin promote passive renal tubular reabsorption due to increased ph.

Table 1 Continued

CASE 11	α– blocker narcotics, CCB's	Nifedipine increases digoxin effect by p-glycoprotein (mdr1) efflux transporter; nifedipine may decrease digoxin clearance, increasing plasma concentrations and the risk of toxicity.	Adjust the digoxin doses as needed.
CASE 12	Serotonin and norepinephrine reuptake inhibitors (SNRIs) with Angiotensin II Receptor Antagonists + anti-platelets + anti- spastic agents	Duloxetine increases clopidogrel effect by pharmacodynamics synergism; SNRIs affect platelet activation; SNRIs with clopidogrel increases bleeding; duloxetine increases nevibolol effect affecting hepatic enzyme CTP2D6 metabolism; telmisartan and nevibolol increases serum potassium; telmisartan increases atorvastatin toxicity (OATP1B1)inhibitor may increase risk of myopathy).	Pregabalin + duloxetine cause pharmacodynamics synergism; co-administration of CNS depressants result in fatal respiratory depression; use the lowest dose as possible and monitor for respiratory depression and or sedation.

The current study (table 3) above considered representation samples as selective descriptive study for elevated number of prescribed drugs of the order of >10 medications per case with chronic illness burden. Geriatrics with failing or progressive decline in homeostatic mechanistic responses with ageing often find hard in reaching therapeutic goals encountering pharmacological alterations of physiological functions in long term therapy and this deserved concern, care, detection, consideration and addressal. For best clinical and humanistic comfort outcomes, critical role of pharmacists in managing medication therapy through monitoring and patient education clear, structured approach is vital and binding. By observing the medication – related morbidities and even mortalities, all established drug mechanistic interactions, prescription combinations with potential for clinically important drug interactions, basic life supporting respiratory depressions, regression of defensive health reflexes, susceptibility to poor physical and mental health, possible physiological interactions that resulted in diminished therapeutic effect of drugs, vital monitoring indices requisites, identified therapeutic priorities were all tabulated within the selected 12 high -polypharmacy case studies.

DISCUSSION

Older patients are generally at higher risk of adverse interactions due to various factors like polypharmacy, co-morbidities and age-related physiological changes that may cause variable effect on pharmacokinetic and pharmacodynamics properties of therapeutic drugs. With a view of adverse interaction risks outweighing beneficial therapeutic outcomes. Polypharmacy is one of the strongest factors increasing the risks of drug–drug interactions, drug–disease interactions, and inappropriate dosing. Polypharmacy are common in geriatric patients and can result in patient morbidity and mortality. More the number of drugs and polypharmacy more will be the number of clinical or pharmacological risk factors significantly contributing to the risk in patient's life. The prevalence of chronic diseases for which one or more medications will be used, increases as one ages, and as number of medicines increase, incidence of inappropriate medicines increases as well. Female gender, polypharmacy and the number of drugs per prescription are independent predictors of inappropriate prescribing.

Research evidence from literature review reveals that more drugs a patient is exposed to, the more likely they are to be prescribed inappropriately [10]. One of the causes for an increase in number of prescription drugs are new medication that are prescribed to treat a side effect that has been misdiagnosed as a new illness. Potentially inappropriate medications in the elderly include those with sedative or anticholinergic effects and long acting non-steroidal anti-inflammatory drugs (NSAIDs) [11]. On the other hand, females are at higher

risk of having inappropriate prescriptions than males.

Polypharmacy may have negative impacts on patients and health care system. In quantitative terms, poly-medication is defined as various drugs simultaneously taken by a patient. Our study used Beers Criteria, a panel-produced list of medications considered inappropriate for older patients, either because of ineffectiveness or high risk for adverse events. Medications were normally designated in one among three categories: people who should be avoided (e.g., barbiturates, chlorpropamide); people who are potentially inappropriate in older adults with particular health conditions or syndromes; and those that should be used with utmost caution. Beer's criteria for potentially inappropriate medication use in older adults was exercised and functionalized to list out the excessive therapeutic agents, minimize the therapeutic regimen and resulting optimize patient compliance towards a sustainably prescribed therapy by the American Geriatric Society.

In the present study, the presence of certain chronic conditions in older patients predicted the increased chance of PIMs use including diabetes, IHD, HF, CKD, cancer, osteoarthritis, osteoporosis, and anxiety which have similar observation using the 2015 American Geriatrics Society Beers criteria [14]. Multiple studies have demonstrated a significant association between PIMs use and cardiovascular diseases, diabetes, osteoporosis and increase number of chronic diseases. [15]

CONCLUSIONS

From the study, it is concluded that the identified drugs were not appropriate as per American Society of Beer's geriatric guidelines 2019. It also showed that one-third of the geriatric patients prescribed with polypharmacy were found to have major drug-drug interactions, suggesting that daily routine pharmacist interventions and patient interaction can play a major role in identifying and assessing drug-drug interactions in geriatric patients.

REFERENCES

1. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. Arch Intern Med. 2002;162:2269–76.
2. Fulton MM, Allen ER. Polypharmacy in the elderly: a literature review. J Am Acad Nurse Pract. 2005;17:123–32.
3. Shah BM, Hajjar ER. Polypharmacy, adverse drug reactions, and geriatric syndromes. Clin Geriatr Med. 2012;28:173–86.
4. Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. Am J Geriatr Pharmacother. 2007;5:345–51.
5. Jokanovic N, Tan EC, Dooley MJ, Kirkpatrick CM, Bell JS. Prevalence and factors associated with polypharmacy in long-term care facilities: a systematic review. J Am Med Dir Assoc. 2015; 16:535 e1–12.
6. Kojima T, Akishita M, Kameyama Y, et al. High risk of adverse drug reactions in elderly patients taking six or more drugs: analysis of inpatient database. Geriatric Gerontol Int. 2012b; 12:761–2.
7. American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc.2012;60(4):616-31.
8. American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers Criteria for potentially inappropriate medication use in older adults. Am Geriatric Soc.2015;63(11):2227-246.
9. Reich O, Rosemann T, Rapold R, Blozik E, Senn O. Potentially inappropriate medication use in older patients in swiss managed care plans: prevalence, determinants and association with hospitalization. PLoS One.2014;9(8):23–5.
10. Fick D, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: Results of a US consensus panel of experts. Archives of Internal Medicine. 2003;163:2716–2724.

11. C. D. Venturini 1, P.Engroff, L.S.Ely, L.F. de Araújo Zago, G.Schroeter, I.Gomes, G.A.De Carli,
12. F. B. Morrone 2011. Gender differences, polypharmacy, and potential pharmacological interactions in the elderly 2011;66(11):1867-72.
13. Rankin, A., Cadogan, C., Patterson, S., Kerse, N., Cardwell, C., Bradley, M., Ryan, C. and Hughes, C., 2018. Interventions to improve the appropriate use of polypharmacy for older people. Cochrane Database of Systematic Reviews,.
14. AlhawassiT, AlatawiW, AlwhaibiM. Prevalence of potentially inappropriate medications use among older adults and risk factors using the 2015 American Geriatrics Society Beers criteria. BMC Geriatrics. 2019;19(1).
15. VieiradeLimaTJ, GarbinCAS, GarbinAJÍ, SumidaDH, SalibaO. Potentially inappropriate medications used by the elderly: prevalence and risk factors in Brazilian care homes. BMC Geriatr. 2013; 13(1):52.

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