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Potentially inappropriate medications in geriatric patients attending a tertiary care hospital in South India: an observational cross-sectional study

Amberkar Mohanbabu Vittalrao[1], Neha Reddy[2], Shreya Hegde[2], Sutanka Sujaini[3], Meena Kumari Kamalkishore[2]

[1]The Oxford Medical College, Hospital and Research Centre, Department of Pharmacology, Bengaluru, India
[2]Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Department of Pharmacology, Manipal, India
[3]Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Department of Obstetrics and Gynaecology, Manipal, India

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Corresponding Author:
Meena Kumari Kamalkishore, M.D., Assoc. Prof., Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Department of Pharmacology, Manipal, India
meena.kumari@manipal.edu

ORCID:
orcid.org/0000-0002-1506-1442

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ABSTRACT

Aims: The aim of this study was to assess drug therapy, possible drug-drug interactions, and potentially inappropriate medications (PIMs) in the geriatric age.

Methods: This was a cross-sectional study with prospective enrollment for 12 months. The study population consisted of geriatric patients admitted to the general medicine department. We defined polypharmacy as the concurrent use of more than 5 medications daily. The American Geriatrics Society Beers 2019 criteria were used to identify PIMs. Drug-drug interactions were identified using a drug interaction checker and categorized into mild, moderate, and severe.

Results: The study included 96 patients (mean age: 70.5±7.8 years, men: 61.5%). Seventy-three patients (76.0%) had polypharmacy. A total of 73 (12.1%) PIMs were identified. Among the 605 medications prescribed 63 (10.4%) potential drug-drug interactions were identified. The percentages of mild, moderate, and severe interactions were 43.5%, 43.5%, and 12.9%, respectively.

Conclusions: In this Indian setting study, while the rate of polypharmacy was high, the rate of PIMs and drug-drug interactions were lower. Vigilance is required to identify drug interactions and PIMs in older adults to avoid adverse drug effects.

Introduction

The world has witnessed the phenomenon of population aging as never before. Initially, an increase in the older adult population was seen only in developed countries; however, even developing countries are having the same challenge. The World Health Organization (WHO) states that by 2050, 80% of older adults will live in low-and middle-income countries. The 2011 population census found that there are nearly 104 million older adults (aged 60 years or above) in India, consisting of 53 million women and 51 million men. The proportion of older adults increased from 5.6% in 1961 to 8.6% in 2011. The United Nations World Population Aging Report 2019 asserts that population

aging is a human success story, reflecting the advancement of public health, medicine, economic, and social development and their contribution to disease control, injury prevention, and reducing the risk of premature death. Simultaneously, this also draws our attention to the need for better healthcare services for older adults. In this era of advancements in the medical management of diseases, one of the challenges faced by physicians in the field of geriatric care is the increased number of medications prescribed for multiple ailments, which results in polypharmacy. Polypharmacy refers to the simultaneous use of multiple medications, including prescription medications, over-the-counter medications, and complementary medications (1). There is a lack of a universally accepted cutoff for the number of drugs to define polypharmacy. The numbers range from ≥2 to ≥11 drugs in various sources. However, concurrent use of more than 5 medicines is one of the most followed definitions (2). Polypharmacy increases the risk of adverse drug events, unfavorable drug interactions, and medication non-adherence (3). It is also associated with increased hospitalization, falls, frailty, cognitive impairment, and mortality in geriatric patients (4). Additionally, potentially inappropriate medications (PIMs) in older adults aggravate the risk of adverse events. PIMs refer to the medication prescribed to a patient in whom the risk of the drug outweighs the benefit (3,5). The increase in morbidities with the passing age contributes to polypharmacy and the use of PIMs. Recent studies have shown an increased incidence of frailty associated with the prescription of PIMs (6-8). A systematic review and meta-analysis by Ma et al. (9) concluded with a bidirectional association between frailty and the use of PIMs. The risk of adverse health outcomes, such as adverse drug reactions, hospitalization, and overall mortality, increases with the number of PIMs prescribed, according to the results of a meta-analysis (10). Hence, scrutiny of the medications prescribed to the geriatric population is considered essential. The present study determined the number of medications, potential drug-drug interactions and PIMs in a South Indian sample (11,12).

Methods

This was a cross-sectional study that prospectively enrolled geriatric inpatients from the Department of Medicine of Kasturba Medical College, Manipal, India, a tertiary care hospital. The study was performed from August 2019 through August 2020. The Institutional Ethics Committee of the Kasturba Medical College and Kasturba Hospital approved the study protocol (IEC number: 312/2019, date: 18/06/2020) that was also registered at the Clinical Trial Registry of India (CTRI/2019/07/020438). Participants provided informed consent and the study protocol conforms to the principles of Helsinki.

The study included men or women aged 60 years or older because the United Nations uses this cutoff to classify elderly (13).

The data were collected from the medical records. The study followed three phases:

Phase 1

We first reviewed the case sheets of all older adult patients aged >60 years admitted to the hospital. The primary cause (s) of admission, comorbidities, drugs, and any adverse drug reactions or drug-drug interactions were recorded. Polypharmacy was defined as the concurrent use of more than 5 medications daily (1,2). We also followed the definition given by Kaufman and group (14), who categorized the patients into four groups of medication count <4, 5-9, 10-14 and >15.

Phase 2

The drugs entered in the first phase were categorized or tabulated according to the Beers screening tool to alert doctors to right treatment (START)/screening tool of older persons' prescriptions (STOPP) criteria (11,12).

Phase 3

Medical review and clinical evaluation were performed based on the number of adverse drug reactions, drug interactions, and possible recommendations for drugs/therapy/regime according to the Beers Criteria (11,12).

Considering prescription details from patient records, the prevalence and frequency of drug-drug interactions and potentially dangerous drug interactions were assessed using computer-based checks available online on the internet (15). Drug interactions were recorded with the following information: drug name, the drug (s) it is interacting with, and the severity of the drug interaction. The severity of drug interactions was graded as mild, moderate, and severe as follows:

Mild: Minimally clinically significant. Minimize risks; assess risks and consider alternative drugs; take steps to circumvent interactions; and/or establish a monitoring plan.

Moderate: Moderately clinically significant. Typically, avoid combinations; use only under special circumstances.

Severe: Highly clinically significant. Avoid combinations; the risk of interaction outweighs the benefit.

Statistical Analysis

The required sample size was calculated with the WHO Epi Info software using the formula $n=4\ pq/d^2$ (n=sample size, p=proportion anti-cipated to have participation in the study, q=1-p, d=absolute precision). With a 50% of participation rate and a relative certanity of 10% at a 95% confidence level, a minimum number of 96 patients was required.

The collected data were recorded as a Microsoft Office Excel 2016 and analyzed using Jamovi version 2.3 statistical software. The descriptive statistics used were proportions and percentages. Mann-Whitney U test was used to compare the average number

of drugs between the two sexes. The Kruskal-Wallis test was used for comparisons across three or more groups. A p value of <0.05 was considered statistically significant.

Results

The study included 96 patients (mean age: 70.5±7.8 years, men: 61.5%). Fifty-six patients (58.3%) had hypertension, 40 (41.6%) had diabetes mellitus, and 12 (12.5%) had chronic kidney disease (CKD) and chronic obstructive pulmonary disease (COPD).

a. Polypharmacy

The percentage of patients on ≤4, 5-9 and ≥10 medications was 23.9%, 69.7% and 6.3%, respectively (Table 1). According to the Kaufmann criteria, the prevalence of polypharmacy (defined as prescription of ≥5 drugs) was 76.1%.

Among patients having polypharmacy, 93.1% were between 60 and 80 years of age (Table 1). There was no statistically significant difference in the number of medications prescribed across age groups (60-70 years, 70-80 years and >80 years) (p=0.580). Similarly, there was no statistically significant difference between sexes (p=0.440).

b. Drug interactions

Using the Beers Criteria (11,12) and a drug interaction checker, the potential drug interactions were predicted and classified as mild, moderate and severe. We identified 63 (10.4%) potential drug interactions. Of them, 43.5%, 43.5% and 12.9% were mild, moderate and severe, respectively. Pantoprazole-cyanocobalamin (9.7%) and aspirin-furosemide (9.7%) were the most frequently noted mild interactions. The most frequent moderate interactions were those of aspirin-furosemide and aspirin-sodium bicarbonate, accounting for 11.1% of the total moderate interactions. Table 2 shows the drugs associated with severe interactions. Among the serious drug interactions, azithromycin-ondansetron interaction had a higher frequency.

Table 1. Distribution of patients according to number of medications and age-group distribution of polypharmacy

Distribution of patients according to the number of medications	
Number of medications	Number (%)
≤4 medications	23 (23.9)
≥5-9 medications	67 (69.7)
≥10 medications	6 (6.3)
Age wise distribution of polypharmacy among patients (total patients on polypharmacy=73)	
Age group(years)	n (%)
60-70	39 (53.4)
71-80	29 (39.7)
81-90	5 (6.8)

c. Potentially inappropriate medications

The total number of PIMs identified in the collected data was 73 (12.1%). The number of repeated PIMs was 20 (27.4%). The most frequently identified PIMs were diuretics (70.8%), tramadol (29.2%), and levetiracetam (19%), followed by aspirin (14.3%) (Tables 3, 4).

Furthermore, the PIMs were categorized as inappropriate for most adults (Table 3), drugs inappropriate for certain diseases (kidney disease) (Table 4), and drugs to be used with caution (Table 4).

Discussion

This study was conducted among patients aged 60 years who were admitted to medical wards to assess polypharmacy, PIMs, and potential drug interactions. The prevalence of polypharmacy was 76.0%. Out of these, most patients (91.8%) fell in the category of 5 to 9 drugs. The remaining patients were prescribed ≥10 drugs. The prevalence of polypharmacy in older adults varies widely across regions, health conditions, and healthcare settings. A cross-sectional analysis conducted on the age group >65 years in 17 European countries and Israel showed a prevalence of polypharmacy in the range of 26.3-39.9% (16). In a prospective cohort of individuals aged >65 years in Sweden, the prevalence of polypharmacy and excessive polypharmacy (>10 drugs) was 44% and 11.7%, respectively (17), while a study on Koreans aged >65 years reported a prevalence of 86.4% (18). We found a high prevalence of polypharmacy in our study sample, similar to previously conducted studies. The WHO recommends that the average number of medications an older adult should take is between 1.3 and 2.2 (19). The average number of drugs in the present study was 6.3, much higher than the recommended number.

The comorbidities commonly associated with geriatric patients with polypharmacy in our study were type 2 diabetes mellitus, hypertension, CKD, and COPD. This finding is in agreement with a previously reported higher rate of polypharmacy in diabetes, hypertension, and heart disease (20). According to a study conducted by Hosseini et al. (21), hypertension, depression, and dementia were the most prevalent diseases associated with polypharmacy. In our patients, CKD and COPD were recorded at high rates.

Most interactions we identified were of mild or moderate grade, not requiring discontinuation. The most common interactions were pantoprazole-cyanocobalamin (the former reduces the gastrointestinal absorption of latter), aspirin-furosemide (aspirin reduces furosemide's action by pharmacodynamic antagonism), aspirin-furosemide (aspirin increases and furosemide reduces serum potassium levels; final effect being unpredictable) and aspirin-sodium bicarbonate (aspirin level increases in parallel with augmented tubular

Table 2. List of drugs associated with severe drug-associated interactions

Drugs with severe interactions	Interaction	Number (%)
Azithromycin x ondansetron	The QTc interval increases	3 (33.3)
Clonidine x diltiazem	Sinus bradycardia	1 (11.1)
Ondansetron x nortriptyline-pregabalin	The QTc interval increases	1 (11.1)
Heparin x warfarin	Increased anti-coagulation bleeding	1 (11.1)
Methylprednisolone x tolvaptan	Methylprednisolone decreases the effect of tolvaptan	1 (11.1)
Clopidogrel x rabeprazole	Rabeprazole decreased the effects of clopidogrel	1 (11.1)
Ceftriaxone x enoxaparin	Ceftriaxone enhances the anti-coagulant effect of enoxaparin	1 (11.1)

Table 3. Medications inappropriate for most adults

Drug	Number (%)
Levetiracetam	8 (19)
Aspirin (in cardiac disease)	6 (14.3)
Glimepiride	5 (11.9)
Clonidine	4 (9.5)
Pregabalin	4 (9.5)
Digoxin	3 (7.1)
Ibuprofen	2 (4.8)
Pentazocine	2 (4.8)
Lorazepam	2 (4.8)
Quetiapine	2 (4.8)
Clonazepam	2 (4.8)
Escitalopram	1 (2.4)
Amiodarone	1 (2.4)

Table 4. Potentially inappropriate medications in drug-disease interactions that may exacerbate the disease and drugs to be used with caution

Drug-disease (kidney disease)	
Drug	**Number (%)**
Dabigatran	3 (42.9)
Enoxaparin	2 (28.6)
Duloxetine	1 (14.3)
Ciprofloxacin	1 (14.3)
Drugs to be used with caution among older adults	
Drugs	Number (%)
Diuretics (spironolactone, furosemide, eplerenone)	17 (70.8)
Tramadol	7 (29.2)

reabsorption due to increased pH by sodium bicarbonate). Among the severe drug interactions, azithromycin-ondansetron was prescribed to three patients. The concurrent use of these two drugs that cause QT interval prolongation may carry a risk of ventricular arrhythmia.

Previous studies have shown that the most common drugs involved in drug interactions were those used to treat cardiovascular diseases and psychotropic agents (22-25). Similarly, the present study showed that drugs used for cardiovascular diseases, specifically anti-thrombotic agents, were involved in the majority of the drug interactions.

The most common PIMs were diuretics, levetiracetam, and tramadol. Notably, medications such as digoxin, diuretics, and tramadol were labeled for use with caution in patients with kidney disease, while others like aspirin (in cardiac disease) and dabigatran were indicated as potentially inappropriate due to their interactions with specific conditions. In a previous study conducted in a similar setting, proton pump inhibitors and anti-histamines comprised the majority of PIMs (26). According to a systematic review of the global prevalence of PIMs among older adults, benzodiazepines were the top prescribed drug class (27). Similarly, a population-based cohort study reported benzodiazepines, followed by proton pump inhibitors, as the most common PIMs in older adults (28). However, in the present study, diuretics, levetiracetam, and tramadol were the most common PIMs. We analyzed PIMs using the American Geriatrics Society 2019 Updated AGS Beers Criteria (11,12) that may not be most suitable for an Indian setting. On the other hand, it should be noted that the American Geriatrics Society Beers Criteria was updated subsequently in 2023 (29).

This study aimed to obtain data with the help of structured proforma and analyze the same data to examine the medications prescribed to the geriatric population to minimize adverse drug reactions by cross-checking the lists and informing physicians of any potentially inappropriate combinations. The prescribers appreciated the report provided on potential drug interactions and PIMs as it would make them more vigilant and aware of several drug interactions and inappropriate medications generally overlooked. Integrating tools like the Beers Criteria and drug interaction checkers into hospital ordering systems could serve as invaluable resources, providing real-time alerts and enabling informed decision-making for safer medication dispensation. While it is used in the United States, its adoption in other countries could significantly enhance medication safety practices, providing proper adaptation and integration into existing healthcare infrastructures. Other tools available to assist in the evaluation of medication regimens like STOPP and START

criteria, Turkish inappropriate medication use in the elderly criteria, and ARMOR (Assess, Review, Minimize, Optimize, Reassess), can be implemented according to the suitability of the health care setting and put into practice (30-33). Moving forward, systematic medication reviews and educational initiatives for healthcare providers can further improve prescribing practices and promote patient safety in geriatric care settings.

This study has several limitations. First, the data collection was difficult in some instances because of the coronavirus disease. Second, although the sample size was not small, outcome rates, particularly the rate of PIMs, were low. Third, the tools to assess drug interactions and PIMs were not validated in the local context. Fourth, the results may not be generalized to other populations and settings, including primary and secondary care facilities.

Conclusion

In this Indian setting study, the rate of polypharmacy was high, but the rate of PIMs and drug-drug interactions were low. Hence, scrutiny of the medication list in older adults is of utmost importance to check for PIMs, polypharmacy, and drug interactions to provide the maximum benefit of the medications, avoid adverse drug effects, and minimize health care costs. Continuing medical education programs may help alleviate prescriptions of PIMs in geriatric patients.

Ethics

Ethics Committee Approval: The study was approved by the Institutional Ethics Committee of Kasturba Medical College and Kasturba Hospital (IEC number: 312/2019, date: 18/06/2020).

Informed Consent: Informed consent was obtained from the participants.

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Footnotes

Authorship Contributions

Concept: A.M.V., M.K.K., Design: A.M.V., M.K.K., Data Collection or Processing: N.R., S.S., Analysis or Interpretation: A.M.V., N.R., S.S., M.K.K., Literature Search: A.M.V., N.R., S.H., S.S., Writing: A.M.V., N.R., S.H., S.S., M.K.K.

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