Original Article

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Patterns and Outcomes of Polypharmacy and Effect of Potentially Inappropriate Medications in Elderly Patients undergoing Orthopaedic Surgeries: A Retrospective Observational Study

Pharmacology Section

SARA YOHANNAN[1], SERAH JOHNY[2], SARA KORULA VERGIS[3], CELINE THALAPPILLIL MATHEW[4]

ABSTRACT

Introduction: Prescription of Potentially Inappropriate Medication (PIM) among elderly patients is becoming a global concern. There has been an increase in the number of elderly patients coming for operative procedures, especially in orthopaedic surgery, due to the association of advanced age with chronic musculoskeletal conditions, such as osteoarthritis, and an increased incidence of fragility fractures.

Aim: To determine the prevalence of polypharmacy and PIMs among elderly patients undergoing orthopaedic surgery.

Materials and Methods: A retrospective observational study was conducted from February 2022 to April 2022 in the Orthopaedic Department of Anaesthesiology, MOSC Medical College, Kolenchery, Ernakulam, Kerala, India. Hospital records of 130 patients aged 65 years and above, who underwent orthopaedic surgeries from January 2016 to December 2021, were included. The prescriptions during the perioperative period were analysed for polypharmacy, defined as the use of five or more drugs. The American Geriatric Society (AGS) 2019 Beers criteria were used to identify PIMs, drug interactions, and drug-syndrome interactions. Chi-square tests were performed on clinically significant variables to assess their effect on hospital stay, with a p-value of <0.05 considered significant.

Results: Polypharmacy was highest on postoperative day 1, with 119 patients (91.5%) experiencing it. The study observed a high prevalence of PIMs, with 106 patients (81.53%) affected. The most commonly used PIMs were Pantoprazole, followed by Piroxicam, Regular human Insulin, and Glimepride. A significant association was observed between hospital stay ≥10 days, postoperative Intensive Care Unit (ICU) stay, and preoperative polypharmacy (p-value=0.002).

Conclusion: Polypharmacy and PIMs in patients above 65 years of age admitted for surgeries remain major concerns. Further exploration of current pharmacologic practices in the perioperative period and interventions, such as physician education programs regarding PIMs, are needed.

Keywords: Beers criteria, Drug interactions, Geriatric, Orthopaedics, Prevalence

INTRODUCTION

The World Health Organisation (WHO) predicts that between 2015 and 2050, the proportion of the world's population over 65 years will be nearly 22%, outnumbering children younger than five years [1]. Healthcare and social systems must be prepared to address this demographic shift. There has been an increase in the number of elderly patients undergoing operative procedures, particularly in orthopaedic surgery, due to the association of advanced age with chronic musculoskeletal conditions such as osteoarthritis and an increased incidence of fragility fractures [2,3]. Additionally, advancing age is associated with multiple co-morbidities like Diabetes Mellitus (DM), Hypertension (HTN), coronary artery disease, chronic renal and pulmonary diseases, arthritis, etc., which make polypharmacy inevitable [3].

Polypharmacy, defined as the use of five or more medications and/or the administration of more medications than clinically indicated, represents unnecessary drug use and is a concern for this population. Aging can significantly alter pharmacokinetic and pharmacodynamic qualities, such as changes in body composition and reductions in kidney and liver function. This often leads to drug-drug interactions and a disproportionately high rate of Adverse Drug Reactions (ADRs) [4]. Polypharmacy increases the risk of drug-related events such as falls, confusion, and functional decline in the elderly. Therefore, the appropriateness of polypharmacy needs to be analysed using different criteria, including Potentially Inappropriate Medications (PIMs), medication underuse, and medication duplication [4].

The PIMs are medications that should be avoided or used with caution, or their dose should be optimised in the elderly, as the risks outweigh the benefits due to the physiology of old age, drug-drug interactions, or drug-disease interactions. Inappropriate prescribing in elderly patients has become a public health concern due to its high prevalence and associated adverse effects, such as ADRs, morbidity, hospitalisation, healthcare utilisation, and increased costs [5]. The search for PIMs was based on the 2019 updated AGS Beers criteria, developed as a tool to improve medication safety in elderly patients [5].

Literature has shown a high prevalence of polypharmacy in the elderly population of India [6]. However, there is limited knowledge about how polypharmacy affects outcomes after orthopaedic surgery. Therefore, the present study aimed to determine the prevalence of polypharmacy and PIMs among elderly patients (>65 years) undergoing orthopaedic surgery in a tertiary teaching hospital using the 2019 updated AGS Beers criteria. This study is aimed to assess the effect of preoperative polypharmacy on postoperative complications and hospital stay in these patients [5].

MATERIALS AND METHODS

The present retrospective observational study was conducted in the Orthopaedic Department of Anaesthesiology, MOSC Medical College, Kolenchery, Ernakulam, Kerala, India from February 2022 to April 2022. Ethical approval, numbered MOSC/IEC/620/2022, with a waiver of written informed consent, was obtained from the Institutional Review Board/Ethics Committees.

Inclusion criteria: The study included hospital records of 130 patients aged 65 years and above who underwent orthopaedic surgeries from January 2016 to December 2021.

Exclusion criteria: Patients with incomplete information about their drugs in medical records and patients with concomitant surgeries other than orthopaedic surgery in the same admission were excluded from the study.

Sample size calculation: The sample size was calculated based on the primary objective of finding the prevalence of polypharmacy. A pilot study was conducted using 20 case records, and the sample size was estimated to be 126 patients using the formula:

$$n=\frac{Z^2_{1-\alpha/2}pq}{(p\varepsilon)^2}$$

Where,

p- Anticipated proportion of event

q=1-p

ε-Precision

$Z_{1-\alpha/2}$- statistical table values

p=0.761 (from pilot study)

q=1-p

ε=10%

$Z_{1-\alpha/2}$=0.7696 (at 5%α)

Then, n=125.6

Minimum sample size, n=126

Study Procedure

A manual review of patients' medical records with a structured data extraction form was conducted. The medications prescribed were analysed according to the 2019 Beers criteria. The data were de-identified by coding to maintain confidentiality. The variables included in the form were age, gender, associated chronic co-morbidities, medications prescribed with dose during the perioperative period, type of surgery (elective/emergency), site of surgery (upper limb/lower limb), American Society of Anaesthesiologists classification (ASA class) [7], and type of anaesthesia (general or local anaesthesia).

The perioperative period was defined as the day of admission to the day of discharge for the study group and was classified into:

→D1- Preoperative day

→D2- First postoperative day

→D3- Date of discharge/deceased

The prescriptions were analysed on D1, D2, and D3 for polypharmacy, which was defined as the use of five or more drugs. The 2019 AGS Beers criteria, an explicit list of Potentially Inappropriate Medications (PIMs) typically best avoided by older adults in most circumstances or under specific situations, was used to identify PIMs, drug-syndrome interactions, and drug-drug interactions. Postoperative outcomes, including hospital stay and ICU days, were recorded.

STATISTICAL ANALYSIS

All data analysis was performed using Microsoft excel and SPSS Statistical Package for Social Sciences version 18.0 (SPSS Inc., Chicago, IL, USA). Categorical data were summarised using frequency and percentage. Continuous variables that followed a normal distribution were summarised using mean and Standard Deviation (SD). To identify the association between polypharmacy and hospital stay, the data was divided into two groups based on a hospital stay of more than or equal to 10 days, and a Chi-square test was performed. A p-value of less than 0.05 was considered statistically significant for all tests.

RESULTS

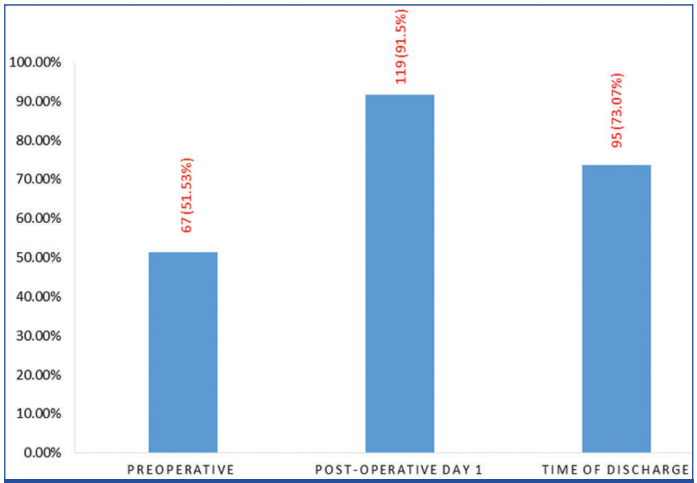
The study included 130 participants above the age of 65 years who underwent orthopaedic surgeries from 2016 to 2021. The mean age of the population was 72.63±7.87 years. Of the participants, 59 (45.4%) were males and 71 (54.6%) were females [Table/Fig-1].

Characteristics	
Age (Mean±SD) (years)	72.63±7.87
Males/Females	59 (45.4%)/71 (54.6%)
ASA I/II/III	5/102/23
Diabetes Mellitus (DM)	59 (45.3%)
Hypertension	78 (60%)
IHD	36 (27.6%)
Chronic kidney disease	8 (6.1%)
Site of surgery UL/LL	38/92
Type of Anaesthesia GA/RA	31/99
Type of surgery Elective/Emergency	102/28

[Table/Fig-1]: Characteristics of study population and surgery.

Out of the total surgeries, 38 (29.2%) were Upper Limb (UL) surgeries and 92 (70.7%) were Lower Limb (LL) surgeries. Among the upper limb surgeries, 19 (50%) were major surgeries, while among the lower limb surgeries, 87 (94.5%) were major surgeries. Among the participants, 106 (81.5%) underwent major surgeries and 24 (18.5%) underwent minor surgeries. Additionally, 102 (78.5%) participants underwent elective surgeries, while 28 (21.5%) underwent emergency surgeries. General Anaesthesia (GA) was administered to 31 (23.8%) participants, while Regional Anaesthesia (RA) was given to 99 (76.1%) participants. The most commonly observed co-morbidities among the participants were hypertension in 78 (60%) patients, Diabetes Mellitus (DM) in 59 (45.3%) patients, and Ischaemic Heart Disease (IHD) in 36 (27.6%) patients. A total of 8 (6.1%) patients had Chronic Kidney Disease (CKD), with two of them undergoing regular haemodialysis.

The prevalence of polypharmacy was highest on the first postoperative day, with 119 (91.5%) participants experiencing polypharmacy [Table/Fig-2]. A total of 9 patients (6.9%) had major polypharmacy, defined as taking more than 10 medications, while 58 patients (44.6%) were taking 5 to 10 medications on the preoperative day [Table/Fig-3]. The prevalence of Potentially Inappropriate Medications (PIMs) in the present study was alarmingly high, with 106 (81.53%) participants using PIMs [Table/Fig-4].



[Table/Fig-2]: Prevalence of polypharmacy according to the various stages of perioperative period.

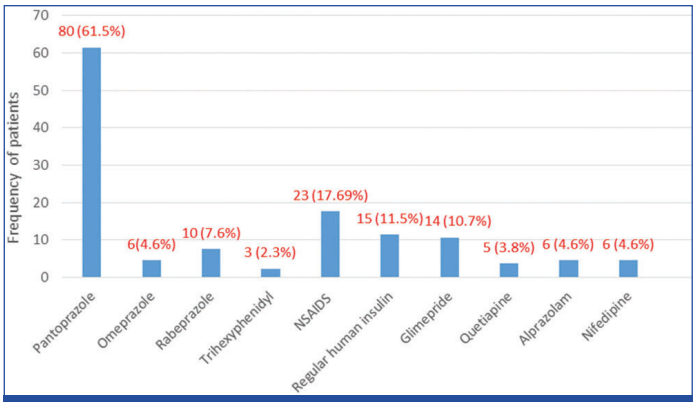
Number of medications on preoperative day	n (%)
<5 medications	63 (48.5%)
5-10 medications	58 (44.6%)
>10 medications	9 (6.9%)

[Table/Fig-3]: Number of medications on preoperative day.
A 58 (44.6%) were on 5 to 10 medications on the preoperative day and 9 (6.9%) were on >10 medications

Variables	Frequencies (%)
PIMS	106 (81.53%)
Drug-drug interaction	15 (11.53%)
Drug-syndrome interaction	4 (3.07%)

[Table/Fig-4]: Prevalence of Potentially Inappropriate Medications (PIMs) and drug interactions among the participants.
Significantly high prevalence of PIMs is seen in the present study

The most commonly used PIMs were pantoprazole (a proton pump inhibitor), followed by piroxicam (a nonsteroidal anti-inflammatory drug), regular human insulin, and glimepiride (a sulfonylurea). Drug-drug interactions were noted with the use of amiodarone and warfarin in a patient with chronic atrial fibrillation, as well as warfarin and etodolac in another patient. Tramadol was used as an analgesic in 80% of patients, along with paracetamol. Non Steroidal Anti-inflammatory Drug (NSAIDs), including piroxicam, etodolac, aceclofenac, and diclofenac, were used in 23 (17.69%) patients on the first postoperative day [Table/Fig-5].



[Table/Fig-5]: Commonly prescribed Potentially Inappropriate Medications (PIMs) among the study group.

A statistically significant association was found between preoperative polypharmacy and hospital stay of 10 days or more, as well as postoperative ICU stay [Table/Fig-6]. No significant association was found between various variables such as emergency surgeries, diabetes, hypertension, and hospital stay duration [Table/Fig-7].

Outcomes	Preoperative polypharmacy		p-value
	Yes	No	
Hospital stay (≥10 days)	32 (69.5%)	14 (30.4%)	0.002
Postoperative ICU stay	35 (61.4%)	22 (38.5%)	0.008

[Table/Fig-6]: Association between preoperative polypharmacy and outcomes.
Chi-square test; p-value <0.05, statistically significant

Variables	Hospital stay duration		p-value
	<10 days	≥10 days	
Emergency surgery	12 (9.2%)	16 (12.3%)	0.534
DM	33 (38.63%)	26 (35.71%)	0.802
HTN	48 (54.54%)	30 (53.6%)	0.935

[Table/Fig-7]: Impact of important variables on hospital stay duration.
Chi-square test; p-value <0.05, statistically significant
No significant association was found between the above variables and hospital stay duration

DISCUSSION

The present study examined the prevalence of polypharmacy and Potentially Inappropriate Medications (PIMs) among older adults undergoing orthopaedic surgeries. The study included 130 patients above the age of 65 years, with 54.6% being females. The prevalence of polypharmacy was found to be 91.5%, while the prevalence of PIMs was 81.53%, which were both alarmingly high. Polypharmacy is common among older adults due to their chronic co-morbidities [8,9]. However, the prevalence of polypharmacy and its association with orthopaedic surgeries and outcomes are underreported.

The study found that the frequency of polypharmacy increased from preoperative to postoperative and discharge stages of hospital stay. On the first postoperative day, 91.5% of patients were on more than five drugs, which could be attributed to the addition of standard antibiotics, analgesics, antiemetics, and Proton Pump Inhibitors (PPIs).

Polypharmacy has been associated with negative consequences such as postoperative complications, functional decline, repeated hospitalisation, and increased mortality [10]. The higher incidence of polypharmacy observed in the present study on the first postoperative day could potentially contribute to these negative outcomes.

The study also identified PIMs using the Beers criteria 2019. The prevalence of PIMs in the present study (81.53%) was higher than in previous studies. In a 201 6 retrospective study of a colorectal cancer surgery population, in patients aged more than 75, the prevalence of PIMs was 26.7% [11]. In the present study, the most commonly prescribed PIMs were PPIs, followed by piroxicam (a non steroidal anti-inflammatory drug), regular human insulin, and Glimepride (Sulfonyurea). [The Beer's criteria advice is to avoid using insulin sliding scale with short- or rapid-acting insulin without concurrent use of basal or long-acting insulin to minimise the risk of hypoglycaemia] [5]. In a similar study done by Sharma R et al., the prevalence of PIM as identified by 201 9 Beers criteria was 61.9% and the most commonly prescribed PIMs were PPI, short acting insulin according to sliding scale, clonazepam and glimepiride [12]. Bhatt A et al., in their study from two teaching hospitals in Southern India, found that the prevalence of polypharmacy was 45.8% and PIMs prescription was 34.0% by 2015 Beers criteria. The most common PIMs in their study are being PPIs followed by benzodiazepines, peripheral alpha-1 blockers, and first-generation antihistamines [13]. According to 2019 Beers criteria PPIs like omeprazole, pantoprazole and rabeprazoles are to be avoided in elderly, as they are associated with the risk of Clostridium difficile infections and increased probability of bone loss and fractures [14-16]. But PPIs are one of the most commonly prescribed drugs for reducing gastric acid secretion, especially in the perioperative period.

The high prevalence of Potentially Inappropriate Medications (PIMs) in the present study (81.53%) was primarily due to the routine use of pantoprazole on the first postoperative day. Pantoprazole is given to reduce gastric acid secretion in patients who are Nil Per Os (NPO) for surgery and to prevent stress-related gastric mucosal damage [17].

Perioperative complications, including gastrointestinal bleeding, can lead to increased morbidity and mortality in elderly patients with hip fractures. The use of PPIs has been shown to significantly reduce Gastrointestinal (GI) bleeding and decrease 90-day mortality in these patients [18,19]. However, it is important to be mindful of drug interactions with benzodiazepines and the potential for electrolyte disturbances when prescribing PPIs to the elderly. PPIs should only be prescribed for appropriate indications, at the lowest effective dose, and for the shortest duration. The need for long-term treatment should be periodically reviewed.

Other inappropriate medications prescribed in the present study included NSAIDs for pain relief. While the majority of patients received tramadol and paracetamol as analgesics, 17.6% were given NSAIDs on the first postoperative day, with a few receiving them preoperatively. Benzodiazepines, regular insulin, and glimepiride were also identified as PIMs in the study group.

Four patients in the study had drug-drug interactions according to the 2019 Beers criteria. One patient was prescribed amiodarone along with warfarin, which can potentially lead to excessive anticoagulation and increased bleeding risk. Other drug interactions included pantoprazole with benzodiazepines, amiodarone with glimepiride, and tramadol with quetiapine.

The study found a significant association between longer hospital stays and preoperative polypharmacy. This is consistent with a study by Abe N et al., which found that polypharmacy at admission was

an independent predictor for prolonged hospitalisation in patients undergoing gastrointestinal surgeries [20]. These results suggest that prescriptions for geriatric patients should take into account their medical history and current medications.

There are multiple criteria available for prescribing drugs in the elderly, such as the Beers criteria and STOPP-START criteria [21]. However, the prevalence of polypharmacy and PIMs in the present study suggests that awareness of these criteria in clinical practice is limited. A comprehensive geriatric assessment should be conducted, evaluating both the individual's functional and medical status. The use of automated warnings may help address inappropriate drugs and drug interactions.

Limitation(s)

One limitation of the present study was that the Beers criteria does not take into consideration a person's overall health, underlying medical conditions, or other specific circumstances that may guide a healthcare provider's choice of medication. Therefore, some of the drugs identified as potentially inappropriate in the present study may not actually be inappropriate in certain cases. Additionally, relying solely on the Beers criteria may not provide accurate results, and the use of additional tools could have potentially reduced the percentage of potentially inappropriate medications.

CONCLUSION(S)

The present study reveals a concerning prevalence of polypharmacy and potentially inappropriate medications in elderly patients (above 65 years of age) admitted for orthopaedic surgeries. The current practices of clinicians in the pharmacological management of elderly patients in the perioperative period should be further investigated, and interventions such as physician education programs should be planned to increase awareness regarding potentially inappropriate medications. The present study aimed to improve clinicians' awareness of the Beers criteria as a tool to enhance medication safety and emphasises the need to establish drug policies regarding the use of potentially inappropriate medications. Strategies for the safe use of medication in the elderly population include setting prescribing limits, using safer alternatives, and discontinuing harmful medications.

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PARTICULARS OF CONTRIBUTORS:
1. Intern, Department of Anaesthesiology, MOSC Medical College, Kolenchery, Ernakulam, Kerala, India.
2. Associate Professor, Department of Pharmacology, MOSC Medical College, Kolenchery, Ernakulam, Kerala, India.
3. Professor, Department of Anaesthesiology, MOSC Medical College, Kolenchery, Ernakulam, Kerala, India.
4. Statistician, Department of Community Medicine, MOSC Medical College, Kolenchery, Ernakulam, Kerala, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Serah Johny,
Associate Professor, Department of Pharmacology, MOSC Medical College, Kolenchery, Ernakulam-682311, Kerala, India.
E-mail: serahjohny@gmail.com

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