Turk J Pharm Sci 2024;21(2):159-166
DOI: 10.4274/tjps.galenos.2023.89457

ORIGINAL ARTICLE

Analyzing the Iatrogenic Triad: Discovering Strategies for Preventing Harm in the Elderly

Vinodkumar MUGADA[1]*, Srinivasa Rao YARGUNTLA[2], Satya Sai Srinivas ALLADA[1], Kamala Kumari PARAVASTU[2], Stephanie Margaret PUVVADA[1]

[1]Vignan Institute of Pharmaceutical Technology, Department of Pharmacy Practice, Duvvada, India
[2]Vignan Institute of Pharmaceutical Technology, Department of Pharmaceutics, Duvvada, India

ABSTRACT

Objectives: The iatrogenic triad is a significant global health problem in the elderly population. This study aimed to evaluate the iatrogenic triad in the elderly and identify potential preventive measures to mitigate its occurrence.

Materials and Methods: A preliminary observational study was conducted on 150 ambulatory elderly patients to assess potentially inappropriate medications (PIMs), polypharmacy, and drug interactions. The AGS Beers Criteria 2019, Polypharmacy, Medication Complexity Regimen Index (MRCI), and Micromedex (a drug information software) were used to assess the harmful triad. Before and after data collection, we observed, identified, and unfolded potential strategies to avoid the harmful triad in the elderly population.

Results: MRCI is 30.49 ± 13.77, suggesting a moderate level of complexity in the drug regimens of elderly patients. Among the PIMs identified by the AGS Beer criteria for 2019, glimepiride (45) and diclofenac (23) were found to be the most frequently prescribed. Moderate-level drug-drug interactions were identified between aspirin and metoprolol (20), metoprolol and metformin (13), and aspirin and enalapril (11). All drug-ethanol and drug-food interactions were rapid and often unknown to patients. Furthermore, the study found that MRCI and polypharmacy were significantly associated with the number of PIMs and drug interactions ($p < 0.01$). Based on data collection, this study identified three possible ways to prevent the iatrogenic triad in elderly patients: interaction, collaboration, and continuing education.

Conclusion: In conclusion, this study sheds light on medication regimen complexity, PIMs, and drug interactions in elderly patients. The study also highlights three possible ways to prevent the iatrogenic triad: interaction, collaboration, and continuing education. By implementing these strategies, healthcare providers can help prevent harm and improve the quality of care for elderly patients.

Keywords: Aged, potentially inappropriate medication list, drug interactions, polypharmacy, medication regimen complexity index

INTRODUCTION

The iatrogenic triad, which consists of potentially inappropriate medications (PIMs), polypharmacy, and drug-drug interactions (DDI),[1] is a significant concern in the field of geriatrics. PIMs refer to the use of a medicine for which the risks outweigh the potential benefits, particularly, when more effective alternatives are available.[2] High prevalence rates of PIM usage (ranging from 18 to over 40%) have been observed across various healthcare settings.[3]

Moreover, older patients frequently use a greater number of medications, leading to polypharmacy. This increased medication use is likely to result in PIM in this population. Furthermore, PIM usage has been associated with hospitalization[4] and mortality,[5] underscoring the importance of addressing this issue in geriatric care.

Co-morbidities and polypharmacy (> 5 medications) are the primary factors contributing to an increased risk of DDI in elderly patients. Furthermore, age-related changes in drug pharmacodynamics and pharmacokinetics may increase the likelihood of developing DDI.[6] To assess the complexity of medication regimens, the medication regimen complexity index (MRCI) is employed. This validated 65-item scoring system considers the number of medications, dosage

*Correspondence: viptpharmd@gmail.com, Phone: +91 7095197222, ORCID-ID: orcid.org/0000-0002-9364-9874
Received: 20.03.2023, Accepted: 06.06.2023

forms, administration instructions, frequency of dosing, and restrictions on food dosing.[7] In addition, polypharmacy and higher medication complexity are responsible for approximately 50% of medication non-adherence rates in elderly patients.[8]

DDIs, such as when anticoagulants intensify blood thinner effects, can increase the MRCI, introducing more variables such as dosage timing. This increased complexity can hinder medication adherence; patient juggling multiple medications might miss doses. Therefore, minimizing DDIs and managing MRCI are crucial to promote adherence, thereby optimizing health outcomes.

To date, no outpatient studies have investigated the impact of pharmacist intervention on the MRCI in the elderly population.[9,10] However, drug interactions, if unavoidable, can be managed through increased awareness and knowledge. In a study by Bories et al.[11] a higher prevalence of PIMs and severe to moderate DDIs were observed in the hospital settings compared with nursing homes and primary care, independent of polypharmacy rates.

To the best of our knowledge, there is a scarcity of research in India that investigates drug-alcohol and drug-food interactions in patients and seeks to identify potential methods to prevent the iatrogenic triad. Our study assessed PIMs, drug interactions, and medication regimen complexity in elderly patients. Through our investigation, we identified three potential strategies that may help prevent or mitigate the harmful triad in this population, emphasizing the need for continued research and intervention development in this area.

Study design, study site, and duration of the study

A descriptive cross-sectional study was conducted on 150 elderly patients attending outpatient departments at a government-funded, 1.000-bed hospital. This facility charges a nominal amount for diagnostic and other medical services while providing necessary medications at no cost to the patients. Owing to its operation in the public sector and its status as one of the major hospitals in nearby regions, the hospital faces a disproportionate doctor-to-patient ratio. The hospital offers surgery and emergency services around the clock. The study spanned six months, from January 7 to July 7, 2022. The manuscript has been reported in accordance with the STROBE guidelines.

Study participants, sampling technique, and sample size estimation

This study focused on elderly patients who were prescribed at least one medication, irrespective of the presence of any co-existing medical conditions. Patients with time constraints were excluded from the study to ensure data reliability. A convenience sampling approach was employed to select each participant, providing a practical and efficient method for participant recruitment. Due to the study's timeline constraints, 150 patients were ultimately included in the research, allowing for a manageable sample size while still offering valuable insights into the topic.

Ethical approval

The Vignan Institute of Pharmaceutical Technology Institutional Human Ethical Committee approved the study (approval no.: VIPT/IEC/89/2022, date: 20.01.2022). The participants were informed of the objectives of the study. We assured the confidentiality of the data and obtained informed consent from each participant.

Study instruments

American Geriatric Society (AGS) Beer's Criteria, 2019[12]

The 2019 AGS Beers Criteria is an update to the 2015 Beers Criteria, providing a comprehensive list of PIMs that should be avoided in elderly patients in specific situations or, in most cases, across the board, particularly when considering certain diseases or conditions. This updated criteria includes a list of PIMs for most older adults, drugs to be avoided for those with certain conditions, DDIs to be aware of, drugs to use with caution, and guidance on dose adjustments in cases of renal failure. For each class of PIMs, the criteria outline the rationale, recommendation, quality of evidence, and strength of recommendation, ensuring a well-informed approach to medication management in geriatric care.

Micromedex[13]

Micromedex is an evidence-based medical information software that serves as a reliable source of drug interaction-related information. To emphasize the importance of addressing these interactions, our study reported drug interactions that exhibited major and moderate severity, rapid and delayed onset reactions, and good and excellent documentation. Nevertheless, in the case of drug-ethanol interactions, we also included results with fair documentation to ensure a comprehensive analysis. Furthermore, we meticulously documented the mechanism of interaction for every instance, highlighting the sophisticated and rigorous approach employed in this academic investigation.

Definitions

Major drug interaction is any life-threatening drug interaction that requires medical intervention to minimize or prevent serious adverse effects. Moderate drug interaction is any drug interaction that may intensify the patient's condition and/or require an alteration in therapy. Excellent documentation indicates that controlled studies have established the existence of the interaction. Good documentation lacks well-controlled studies but strongly suggests an interaction. Fair documentation suspects an interaction based on pharmacological considerations from lead clinicians or documentation is good for a pharmacologically similar drug.

Medication regimen complexity index[14]

The MRCI is a validated, 65-item scale designed to quantify the complexity of a patient's drug regimen. This index considers factors such as the number of prescribed medications, dosage form, frequency of administration, and additional instructions for use. Consequently, a higher MRCI score signifies a more intricate and complex medication regimen, thereby emphasizing the importance of understanding and managing medication complexity in clinical practice.

Outcomes

The primary outcome of this study was to thoroughly analyze the iatrogenic triad, which encompasses PIMs, polypharmacy (> 5 medications), and DDIs. Concurrently, the secondary outcome is to identify effective strategies that can mitigate or prevent harm caused by the iatrogenic triad in elderly patients, ultimately contributing to improved patient outcomes and enhanced quality of geriatric care. Another secondary outcome is to identify medication regimen complexity using MRCI.

Data collection

Data collection was performed in two distinct parts. The initial part encompassed gathering the demographic and clinical details of the patients, such as their age, gender, smoking and alcoholism status, department name, diagnosis of the patient's condition, and the number of prescribed drugs. The subsequent phase involved prescription auditing to identify PIMs, medication regimen complexity, and potential DDIs, following Beer's criteria (2019).

Data analysis

Quantitative data were presented as mean and standard deviation or median and interquartile range, depending on whether the data were normally distributed or not. Qualitative data are presented as frequencies and percentages. To investigate the relationship between MRCI, polypharmacy (> 5 medications), PIMs, and drug interactions, paired-samples *t*-test or Wilcoxon test was used based on the normality assumption. The *p* value, effect size, and 95% confidence interval were reported for the tests. Spearman's Rho correlation was conducted to examine the degree of association between the medication regiment complexity index, polypharmacy, and drug interactions. The level of statistical significance was set at $p < 0.05$.

Statistical analysis

Statistical analysis was performed using Jeffrey's Amazing Statistics Programme software (version 0.14.1.0).

RESULTS

A total of 150 elderly patients participated in the study. Table 1 shows that the mean age of the elderly was 69.30 ± 5.16 years, and the mean score of the MRCI is 30.49 ± 13.77. Nearly more than half of the patients were males (52.67%), with most of them being non-smokers (72%) and non-alcoholics (74.67%). Polypharmacy (use of > 5 drugs) constituted nearly three-quarters of prescriptions (72.66%). A total of 158 DDIs were detected in the patients, and 97.47% of these interactions were moderate DDIs.

According to AGS Beer's criteria, 2019, the most prescribed PIMs are glimepiride (45) and diclofenac (23) (Table 2). The most reported DDIs are aspirin and metoprolol (20), metoprolol and metformin (13), and aspirin and enalapril (11), all with a moderate level of severity of interaction (Table 3).

MRCI and polypharmacy are significantly associated with interactions and the number of PIMs. However, polypharmacy has a significantly positive correlation with the number of PIMs, whereas MRCI has a significantly positive correlation with drug interactions (Table 4). All drug-ethanol and drug-food interactions are rapid, and patients are unaware of them (Table 5).

DISCUSSION

The key results of the study revealed that the mean age was 69.30 ± 5.16 years, and the mean MRCI score was 30.49 ± 13.77. Polypharmacy was present in 72.66%, and 158 DDIs, mostly moderate, were detected. The most common PIMs were glimepiride and diclofenac. MRCI and polypharmacy significantly

Table 1. Distribution of sociodemographic and clinical details of patients (n= 150)

Characteristic	Frequency (%)
Age	69.30 ± 5.16*
MRCI	30.49 ±13.77*
Males Females	79 (52.67) 71 (47.33)
Non-smokers	108 (72)
Smokers Ex-smokers	30 (20) 12 (8)
Non-alcoholics	112 (74.67)
Alcoholics Ex-alcoholics	24 (16) 14 (9.33)
The type of department	
General medicine	74 (49.33)
Endocrinology	39 (26)
Pulmonology	14 (9.33)
Others†	23 (15.33)
Polypharmacy	
< 5	41 (27.33)
5-6	65 (43.33)
< 7	44 (29.33)
Diagnosis	
Hypertension	113 (75.33)
Diabetes mellitus	96 (64)
CAD	15 (10)
COPD	13 (8.66)
Chronic kidney disease	11 (7.33)
Hypothyroidism	10 (6.66)
DDIs (n= 158)	
Major	4 (2.53)
Moderate	154 (97.47)

†= Orthopedics, nephrology, oncology, general surgery, neurology, *mean ± SD, MRCI: Medication regimen complexity index, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, SD: Standard deviation

correlated with DDIs and PIMs, with patients largely unaware of rapid drug-ethanol and drug-food interactions.

A recent study found that individuals with an MRCI score of 22 upon hospital discharge were more prone to unanticipated hospital readmissions within 30 days.[15] Another study indicated that a cut-off score of 33 on the MRCI was optimal in identifying medication-related readmission risks.[16] However, it should be noted that these thresholds may vary based on different contexts. Non-etheless, few studies,[17,18] have consistently demonstrated that polypharmacy, i.e., the use of five or more medications, is a predictor of unplanned hospitalizations.

Wimmer et al.[18] found that older adults living at home who had complex medication regimens and were taking numerous medications were more likely to experience unplanned hospitalizations. The study also revealed that the two predictors, medication regimen complexity and number of medications, had similar sensitivity and specificity in predicting unplanned hospitalizations. These results indicate that it may be possible to use these parameters to anticipate unplanned hospitalizations in the elderly. To support this, the MRCI has been recently proposed as a tool for identifying individuals who may benefit from medication therapy management.[19]

The concept of the iatrogenic triad in the elderly refers to three interrelated elements that can adversely affect the health of older adults: polypharmacy (the concurrent use of multiple medications), DDIs, and the use of PIMs.[20] A study conducted in Brazil explored the prevalence and inter-relationship of these elements in older adults. The research found that a high percentage of the elderly population was exposed to the iatrogenic triad. Specifically, 44.6% experienced polypharmacy, 72.3% were at risk of DDIs, and 42.1% were using PIMs as *per* Beers criterion. Almost one-third (29.3%) of the study participants were exposed to all three elements of the iatrogenic triad simultaneously. The study also found that frailty and having a caregiver were associated with this triad.[20]

Research has demonstrated that the iatrogenic triad is prevalent in the elderly population. For instance, a study on elderly women reported that nearly 90% of the participants used at least one

Table 2. PIMs in prescriptions according to the AGS Beers Criteria, 2019

Name of the medication	Frequency	Rationale	Recommen dation	Quality of evidence	Strength of the recommendation
Glimepiride	45	Older adults are at a higher risk of prolonged hypoglycemia	Avoid	High	Strong
Diclofenac	23	High risk of gastrointestinal bleeding or peptic ulcer disease in individuals taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents. Induces kidney injury and increases blood pressure. Risks are dose-related	Avoid chronic use, unless other alternatives are not effective, and the patient can take a gastroprotective agent (proton-pump inhibitor or misoprostol)	Moderate	Strong
Tramadol	3	May intensify or cause (syndrome of inappropriate antidiuretic hormone) or hyponatremia	Use with caution	Moderate	Strong
Nifedipine immediate release	2	Potential for hypotensionand risk of precipitating myocardial ischemia	Avoid	High	Strong
Alprazolam	2	Age-related cognitive impairment, delirium, falls, fractures, and motor vehicle crashes.	Avoid	Moderate	Strong
Spironolactone	2	Increased potassium if creatinine clearance < 30 mL/min	Avoid	Moderate	Strong
Theophylline	2	Increased risk of theophylline toxicity with cimetidine and ciprofloxacin	Avoid	Moderate	Strong
Chlorzoxazone	1	Older adults have a poor tolerance for most muscle relaxants because of anticholinergic adverse effects, sedation, and fracture risks	Avoid	Moderate	Strong
Levetiracetam	1	CNS adverse effects, creatinine clearance ≤ 80 mL/min	Reduce dose	Moderate	Strong
Glibenclamide	1	Higher risk of severe prolonged hypoglycemia in older adults	Avoid	High	Strong

PIMs: Potentially inappropriate medications, AGS: American Geriatric Society

element of the iatrogenic triad. The study also noted a high index of continuous use medications, PIMs, and potential drug interactions, particularly among enzymatic inhibitors. It was observed that old age was associated with the presence of all elements of the iatrogenic triad, underscoring the importance of vigilant medication management in this population.[21]

According to the 2019 AGS Beer's criteria, more than half of the prescriptions in our study (54.60%) included medications that were inappropriate for elderly patients. Among such medications, the antidiabetic drugs glimepiride and glibenclamide pose a higher risk of prolonged hypoglycemia in the elderly population. The evidence supporting this recommendation is of high quality, and the recommendation itself is strongly endorsed. Prolonged hypoglycemia can lead to adverse outcomes, including bone fractures from falls, seizures, long-term cognitive impairment (such as dementia), frailty, extended hospital stays, and even mortality in hospitals.[22] It is crucial for physicians to be aware of these PIMs to avoid their use in elderly patients. If physicians are aware, there is an opportunity to replace PIMs with alternative drugs where the benefits outweigh the risks.

No scholarly research originating from India has documented any instances of drug-alcohol or drug-food interactions. Our study highlights the rapid onset and potential severity of drug-alcohol and drug-food interactions, ranging from moderate to

Table 3. DDIs according to severity, onset, documentation, and mechanismof action

DDI	Severity	Onset	Documen station	Frequency	Mechanism
Aspirin and metoprolol	Moderate	Delayed	Good	20	NSAIDS and beta-adrenergic blockers may increase blood pressure
Metoprolol and metformin	Moderate	Delayed	Good	13	Beta-blockers may inhibit or increase the blood glucose-lowering effect of antidiabetic agents and may obscure hypoglycemia symptoms
Aspirin and enalapril	Moderate	Rapid	Excellent	11	May result in decreased effectiveness of enalapril
Atenolol and metformin	Moderate	Delayed	Good	10	The blood glucose-lowering effect of an antidiabetic drug may be increased or decreased, and hypoglycemia symptoms may be obscured
Atenolol and glimepiride	Moderate	Delayed	Good	6	It may increase or decrease the blood glucose-lowering effect of the antidiabetic agent and diminish or obscure hypoglycemic symptoms
Aspirin and atenolol	Moderate	Delayed	Good	4	May result in increased blood pressure
Azithromycin and theophylline	Moderate	Delayed	Good	3	May result in increased serum theophylline concentrations
Atenolol and diclofenac	Moderate	Delayed	Good	2	May result in increased blood pressure
Aspirin and nitroglycerin	Moderate	Rapid	Good	2	Increased nitroglycerin levels and additive platelet dysfunction
Clopidogrel and esomeprazole	Major	Rapid	Excellent	1	Reduces antiplatelet activity and plasma levels of clopidogrel active metabolites
Atorvastatin and phenytoin	Moderate	Delayed	Excellent	1	Reduces atorvastatin plasma concentrations and efficacy
Clopidogrel and tramadol	Major	Rapid	Good	1	Reduces the efficacy of clopidogrel

DDI: Drug-drug interactions, NSAID: Non streoidal anti inflammatory drug

Table 4. Association and correlation among variables in the study

Measure 1	Measure 2	*p* value††	Effect size*	95% CI for effect size		Correlation†
				Lower	Upper	r: *p* value
MRCI	No. of PIM	< 0.00001	1.000	1.000	1.000	0.03: 0.773
Polypharmacy	No. of PIM	< 0.00001	1.000	1.000	1.000	0.58: < 0.0001
Polypharmacy	Interactions	< 0.00001	0.950	0.927	0.965	0.005: 0.959
MRCI	Interactions	< 0.00001	1.000	1.000	1.000	0.50: < 0.0001

†Spearman's Rho Correlation, ††Wilcoxon signed-rank test, *Effect size-effect size is given by the matched rank biserial correlation, MRCI: Medication regimen complexity index, PIM: Potentially inappropriate medication, CI: Confidence interval

major. Patients who are not educated on these interactions by a clinical pharmacist are often unaware of the associated risks, which can result in therapeutic failure. For instance, concurrent intake of food can decrease furosemide exposure and efficacy, whereas alcohol consumption while taking aspirin can increase the risk of gastrointestinal bleeding. These interactions are typically unknown to both patients and physicians, underscoring the need for clinical pharmacist involvement in such cases.

Moreover, our study identified three potential strategies to prevent the iatrogenic triad in elderly patients: interaction, collaboration, and continuing education. Notably, we found no previous studies in India that have outlined such systematic approaches for mitigating the risks associated with the iatrogenic triad in the elderly.

Interaction

Patients will have the opportunity to interact with the clinical pharmacist (Figure 1). Typically, patients are required to register as outpatients and then wait to consult with a physician. During this waiting period, the clinical pharmacist will meet the patient and collect the best possible medication history (BPMH) using a standard proforma. The BPMH includes information such as current medications, drugs discontinued within the last six months, drug allergies, over-the-counter medications, alternative medicine, vitamin and mineral supplements, herbal supplements, and recent immunization. The clinical pharmacist will record this comprehensive information in patient case sheets. The patient will then consult with the physician using the updated case sheet. Public hospitals should actively foster collaboration with pharmacy colleges to encourage their participation as stakeholders in the process of mitigating the iatrogenic triad in vulnerable populations such as the elderly. By cultivating a symbiotic relationship between these institutions, a more comprehensive approach can be employed to address and prevent potential complications arising from medical interventions.

Collaboration

Based on the information obtained from the BPMH and drug allergy records provided by the clinical pharmacist, the physician will proceed to prescribe appropriate drugs. The clinical pharmacist will then conduct a thorough review of the prescription to identify PIMs, drug interactions, and instances of polypharmacy. In cases where discrepancies are identified, both the physician and clinical pharmacist will consult established evidence and guidelines to inform their decision-making. Upon reaching a consensus, the physician will proceed to individualize and represcribe the therapy as necessary (Figure 1).

Table 5. Possible drug ethanol and drug-food interactions according to severity, onset, evidence, and mechanism

Drug-ethanol interactions					
Name of the drug	**Severity**	**Onset**	**Documentation**	**Frequency**	**Warning**
Aspirin	Moderate	Rapid	Good	8	A combination of ethanol and aspirin may increase the risk of gastrointestinal bleeding
Nitroglycerin	Moderate	Rapid	Fair	2	Hypertension may result from the concurrent use of nitroglycerin and ethanol
Cetirizine	Major	Rapid	Fair	1	Cetirizine and ethanol may cause CNS depression when used together
Amitriptyline	Moderate	Rapid	Good	1	Amitriptyline and ethanol combined may result in enhanced CNS depression
Tramadol	Major	Rapid	Fair	1	Tramadol and ethanol may cause respiratory and CNS depression when used concurrently
Drug-food interactions					
Furosemide	Moderate	Rapid	Excellent	11	Food and furosemide may reduce the efficacy and exposure to furosemide
Metoprolol	Moderate	Rapid	Excellent	26	Metoprolol concentrations may increase when combined with food
Acetaminophen	Moderate	Rapid	Good	21	Acetaminophen effectiveness may be decreased when used concurrently with cabbage
Theophylline	Moderate	Rapid	Good	4	Food and theophylline may alter theophylline concentrations
Montelukast	Moderate	Rapid	Excellent	4	The use of montelukast and grapefruit juice together may increase montelukast exposure.
Ciprofloxacin	Moderate	Rapid	Good	5	Dairy foods and ciprofloxacin may decrease ciprofloxacin concentrations.

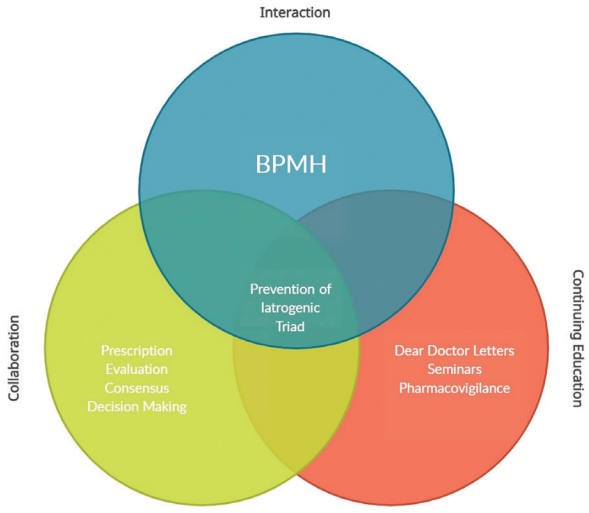

Figure 1. Interaction of outpatients, continuing education, and collaboration of physicians with a clinical pharmacist

BPMH: Best possible medication history

Collaborative interventions between pharmacists and physicians have been shown to improve the medication appropriateness index scores of elderly patients.[23] A collaborative care approach with a focus on pharmacists has been found to be effective in reducing drug-related problems, potential DDIs, and PIMs, as well as improving positive clinical outcomes related to quality-of-life measures in elderly patients with mental health concerns.[24] Moreover, interventions aimed at optimizing medication usage have been successful in reducing the risk of serious adverse drug reactions (ADRs) in older adults.[25] Nonetheless, the acceptability of pharmacist-led interventions as a means of optimizing treatment is a crucial consideration.

Continuing education

Continuing medical education is an essential tool for keeping physicians abreast of new developments and advances in medicine. This education is facilitated through various channels, such as dear doctor letters, seminars and conferences, and pharmacovigilance activities. Dear doctor letters disseminate vital information, including new drug approvals by the FDA, recent inappropriate drug usage in high-risk populations, and ADRs that commonly occur in hospitals. Clinical pharmacist-led seminars and conferences cover diverse aspects of drug safety, whereas pharmacovigilance activities enable unsolicited reporting of ADRs by healthcare and allied healthcare personnel in high-risk populations. The implementation of such measures serves to deter the prescribing or caution the use of drugs that pose potential risks to patient safety (Figure 1).

In the D-PRESCRIBE randomized trial, Martin et al.[26] established a pharmacist-led intervention group aimed at promoting educational deprescribing brochures and providing evidence-based pharmaceutical opinions to physicians. This study focused on older adults in Quebec and compared the outcomes of the intervention group with those receiving standard care. Results revealed that after 6 months, participants who received the educational intervention discontinued prescriptions for inappropriate medications. However, further research is necessary to establish the generalizability of these findings to broader patient populations.

The interplay between these three methods-interaction, collaboration, and continuing education-can significantly minimize the iatrogenic triad in the elderly. The patient-centered approach, coupled with strong professional collaboration and an emphasis on continual learning, forms a robust defense against the potential pitfalls associated with polypharmacy and complex medical care in the elderly population. They form a synergistic approach that addresses various aspects of medication safety and management. Combining these factorscan improve medication-related outcomes, reduce the iatrogenic triad, and enhance the overall well-being of the elderly population.

Study limitations

This study has some limitations. First, the small sample size is small and affects the generalizability of the results. Second, the health policy making of integrating pharmacists into patient care may require feasibility and acceptability of multiple stakeholders. However, considering the benefit of the approach and the significant number of pharmacy colleges in Andhra Pradesh, it may be possible to implement the approach in real time for optimal results.

Potential implications of the study

This study has important implications for improving the quality of care for elderly patients and preventing the iatrogenic triad. By implementing the strategies identified in this study, healthcare providers can reduce the risk of harm and improve outcomes for this vulnerable population.

Improved medication management for the elderly

The study's findings highlight the need for healthcare providers to review and adjust medication regimens for elderly patients to reduce the risk of PIMs, polypharmacy, drug interactions, and medication regimen complexity. This could lead to better health outcomes and quality of life for elderly patients.

Development of clinical guidelines

The study findings could inform the development of clinical guidelines for medication management in elderly patients. These guidelines could provide healthcare providers with a framework for assessing medication regimens, identifying PIMs, and managing drug interactions in elderly patients.

CONCLUSION

We observed the iatrogenic triad in the elderly. The iatrogenic triad in the elderly may be prevented using three possible ways that we observed in our study: interaction of patients with the clinical pharmacist to obtain the BPMH history; collaboration of the clinical pharmacist with physicians for informed decision-making and optimizing the pharmacotherapy; and continuing education activity led by a clinical pharmacist to update the knowledge on drug safety and prescribing in the physicians.

Ethics

Ethics Committee Approval: The Vignan Institute of Pharmaceutical Technology Institutional Human Ethical Committee approved the study (approval no.: VIPT/IEC/89/2022, date: 20.01.2022).

Informed Consent: We assured the confidentiality of the data and obtained informed consent from each participant.

Authorship Contributions

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

Conflict of Interest: The authors have no relevant financial or non-financial interests to disclose.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Novaes PH, da Cruz DT, Lucchetti ALG, Leite ICG, Lucchetti G. The "atrogenic triad": polypharmacy, drug-drug interactions, and potentially inappropriate medications in older adults. Int J Clin Pharm. 2017;39:818-825.
2. Renom-Guiteras A, Meyer G, Thürmann PA. The EU(7)-PIM list: a list of potentially inappropriate medications for older people consented by experts from seven European countries. Eur J Clin Pharmacol. 2015;71:861-875.
3. Motter FR, Fritzen JS, Hilmer SN, Paniz ÉV, Paniz VMV. Potentially inappropriate medication in the elderly: a systematic review of validated explicit criteria. Eur J Clin Pharmacol. 2018;74:679-700.
4. Cabré M, Elias L, Garcia M, Palomera E, Serra-Prat M. Avoidable hospitalizations due to adverse drug reactions in an acute geriatric unit. Analysis of 3,292 patients. Med Clin (Barc). 2018;150:209-214.
5. Muhlack DC, Hoppe LK, Weberpals J, Brenner H, Schöttker B. The association of potentially inappropriate medication at older age with cardiovascular events and overall mortality: a systematic review and meta-analysis of cohort studies. J Am Med Dir Assoc. 2017;18:211-220.
6. Mallet L, Spinewine A, Huang A. The challenge of managing drug interactions in elderly people. Lancet. 2007;370:185-191.
7. Brysch EG, Cauthon KAB, Kalich BA, Sarbacker GB. Medication regimen complexity index in the elderly in an outpatient setting: a literature review. Consult Pharm. 2018;33:484-496.
8. Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. Am J Geriatr Pharmacother. 2007;5:345-351.
9. Elliott RA, O'Callaghan C, Paul E, George J. Impact of an intervention to reduce medication regimen complexity for older hospital inpatients. Int J Clin Pharm. 2013;35:217-224.
10. Stange D, Kriston L, von-Wolff A, Baehr M, Dartsch DC. Reducing cardiovascular medication complexity in a German university hospital: effects of a structured pharmaceutical management intervention on adherence. J Manag Care Pharm. 2013;19:396-407.
11. Bories M, Bouzillé G, Cuggia M, Le Corre P. Drug-drug interactions in elderly patients with potentially inappropriate medications in primary care, nursing home and hospital settings: a systematic review and a preliminary study. Pharmaceutics. 2021;13:266.
12. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019;67:674-694.
13. MerativeTM Micromedex® Drug Interaction Checking (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/
14. George J, Phun YT, Bailey MJ, Kong DC, Stewart K. Development and validation of the medication regimen complexity index. Ann Pharmacother. 2004;38:1369-1376.
15. Schoonover H, Corbett CF, Weeks DL, Willson MN, Setter SM. Predicting potential postdischarge adverse drug events and 30-day unplanned hospital readmissions from medication regimen complexity. J Patient Saf. 2014;10:186-191.
16. Olson CH, Dierich M, Adam T, Westra BL. Optimization of decision support tool using medication regimens to assess rehospitalization risks. Appl Clin Inform. 2014;5:773-788.
17. Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ, McLachlan AJ, Cumming RG, Handelsman DJ, Le Couteur DG. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. J Clin Epidemiol. 2012;65:989-995.
18. Wimmer BC, Bell JS, Fastbom J, Wiese MD, Johnell K. Medication regimen complexity and number of medications as factors associated with unplanned hospitalizations in older people: a population-based cohort study. J Gerontol A Biol Sci Med Sci. 2016;71:831-837.
19. Clay PG. Medication regimen complexity indices: a tool to focus MTM efforts? J Am Pharm Assoc. 2014;54:664.
20. Malabu UH, Vangaveti VN, Kennedy RL. Disease burden evaluation of fall-related events in the elderly due to hypoglycemia and other diabetic complications: a clinical review. Clin Epidemiol. 2014;6:287-294.
21. Novaes PH, da Cruz DT, Lucchetti ALG, Leite ICG, Lucchetti G. The "iatrogenic triad": polypharmacy, drug-drug interactions, and potentially inappropriate medications in older adults. Int J Clin Pharm. 2017;39:818-825.
22. De Oliveira HSB, Gonzales Manso ME. The iatrogenic triad in a group of elderly women contracted to a health plan. SciELO. 2019;22:e180188.
23. Shim YW, Chua SS, Wong HC, Alwi S. Collaborative intervention between pharmacists and physicians on elderly patients: a randomized controlled trial. Ther Clin Risk Manag. 2018;14:1115-1125.
24. Stuhec M, Bratović N, Mrhar A. Impact of clinical pharmacist's interventions on pharmacotherapy management in elderly patients on polypharmacy with mental health problems including quality of life: a prospective non-randomized study. Sci Rep. 2019;9:16856.
25. Gray SL, Hart LA, Perera S, Semla TP, Schmader KE, Hanlon JT. Meta-analysis of interventions to reduce adverse drug reactions in older adults. J Am Geriatr Soc. 2018;66:282-288.
26. Martin P, Tamblyn R, Benedetti A, Ahmed S, Tannenbaum C. Effect of a pharmacist-led educational intervention on inappropriate medication prescriptions in older adults: the D-PRESCRIBE randomized clinical trial. JAMA. 2018;320:1889-1898.