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Study on patient safety and rational use of medicines: Assessment of potential drug interactions in prescriptions for elderly patients

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Abstract

Drug therapy is the most widely used alternative and represents a major advance in the treatment of diseases. However, inappropriate use of medications can aggravate comorbidities and compromise patient safety, becoming a public health problem. Polypharmacy is especially common in the elderly, increasing the risk of drug interactions. **Objectives:** this study aimed to analyze potential drug interactions in elderly patients admitted to the cardiology ward of a university hospital. **Methods:** the drug prescriptions prescribed at admission and discharge of hospitalized elderly patients were evaluated, and drug interactions were checked using two software: Medscape and Drugs.com. **Results:** the most frequent drug interactions, according to the mechanism classification, were pharmacodynamic, both in Drugs.com (89%) and in Medscape (69%). In terms of severity, the most frequent were moderate, both at admission (776) and at discharge (929) in Drugs.com, and in Medscape also 760 (admission) and 904 (discharge). The most prevalent associated drugs were clopidogrel and acetylsalicylic acid (141). Most patients included in the study had more than five prescribed medications (89.14% at admission and 92.12% at discharge), which may be related to the increase in the number of potential drug interactions. **Conclusions:** the present study contributes to the reflection on therapeutic alternatives, dose adjustment and adequacy of drug posology.

Keywords: Potential drug interactions; elderly; polypharmacy.

Estudo sobre segurança do paciente e uso racional de medicamentos: Avaliação de potenciais interações medicamentosas em prescrições para pacientes idosos

Resumo

A terapia medicamentosa é a alternativa mais utilizada e representa um grande avanço no tratamento de doenças. Entretanto, o uso inadequado de medicamentos pode agravar comorbidades e comprometer a segurança do paciente, tornando-se um problema de saúde pública. A polifarmácia é especialmente comum em idosos, aumentando o risco de interações medicamentosas. **Objetivo:** este estudo visou analisar interações medicamentosas potenciais de pacientes idosos internados na enfermaria de cardiologia em um hospital universitário. **Métodos:** foram avaliadas as prescrições medicamentosas de admissão e alta de pacientes idosos internados, as interações medicamentosas foram checadas com o auxílio dos softwares Medscape e Drugs.com. **Resultados:** as interações medicamentosas mais frequentes, de acordo com a classificação de mecanismo, foram as farmacodinâmicas tanto no Drugs.com (89%) quanto no Medscape (69%). Segundo a gravidade, as mais frequentes foram as moderadas, tanto na admissão (776) quanto na alta (929) no Drugs.com, e no Medscape também 760 (admissão) e 904 (alta). Os fármacos mais prevalentes associados foram clopidogrel e ácido acetilsalicílico (141). A maioria dos pacientes incluídos no estudo possuíam mais de cinco medicamentos prescritos (89,14% na admissão e 92,12% na alta), o que pode estar relacionado com o aumento no número de potenciais interações medicamentosas. **Conclusão:** o presente estudo contribui para a reflexão acerca de alternativas terapêuticas, ajuste de dose e adequação de posologia de medicamentos.

Palavras-chave: Potenciais interações medicamentosas; idosos; polifarmácia.

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Introduction

Patient safety has been widely discussed in recent years. Technical committees and regulatory improvements have been implemented to ensure this social right, facilitated by the creation of the World Alliance for Patient Safety by the World Health Organization (WHO)[1]. Following the trend indicated by the WHO, Brazil approved the implementation of the National Patient Safety Program through Ministry of Health Ordinance No. 529, which provided guidance for healthcare professionals regarding necessary patient care[2].

Among patient care measures, medication prescription is particularly relevant. It must be individualized, ensuring that the risks are lower than the benefits for the patient. With this approach in mind, the WHO launched the Third Global Challenge in 2017, under the theme *Medication Without Harm*, aiming to mitigate and raise awareness of serious and preventable medication-related errors[1,3].

Certain factors can increase the likelihood of medication-related harm, such as polypharmacy, defined as the simultaneous use of four or more medications by the same patient[3,4]. It can also be classified as excessive polypharmacy when more than ten medications are prescribed[5]. Polypharmacy is associated with a higher risk of adverse drug events (ADEs) and therapeutic inefficacy[6].

Elderly patients, due to the presence of chronic non-communicable diseases (NCDs) and physiological aging, often require the concomitant use of multiple medications throughout their lives. For this reason, they require special attention when evaluating medication prescriptions[7].

There are different types of medication-related problems, which may be predictable or not. Among the predictable events, potential drug interactions (PDI) stand out[9]. PDIs are defined as drug interactions present in a medical prescription that have been previously documented and recognized. These interactions may or may not have clinical repercussions, potentially compromising pharmacological treatment by increasing toxicity or reducing expected therapeutic efficacy[8-9].

Potential drug interactions (PDIs) can be classified based on their mechanism as either pharmacodynamic or pharmacokinetic. Pharmacodynamic interactions occur when two active substances compete for the same pharmacological target. The expected effect can be synergistic, when both drugs have the same effect on the pharmacological target, or antagonistic, when the drugs have opposite effects on the same receptor or transporter. Pharmacokinetic interactions, on the other hand, can occur during the processes of absorption, distribution, metabolism, or excretion of the drug within the body. Furthermore, PDIs can also be classified according to their severity as mild, moderate, or severe[10-12].

Considering the specificities of cardiology wards, it is crucial for healthcare professionals to remain vigilant regarding elderly patients and potential drug interactions, as well as to understand their mechanisms in order to optimize pharmacotherapy, minimize adverse events, and promote therapeutic efficacy. The objective of this study is to evaluate the potential drug interactions in elderly patients hospitalized in the cardiology ward of a university hospital.

Methods

The admission and discharge prescriptions of patients hospitalized in the cardiology ward of a university hospital in the city of Vitória-ES were analyzed. Data regarding the patients' prescriptions were obtained electronically, ensuring the identity of each patient was protected.

Admission and discharge prescriptions were included for elderly patients (aged 60 years or older) hospitalized in the cardiology ward from January 1 to December 31, 2019. Prescriptions containing fewer than two prescribed medications were excluded, as the evaluation was focused on drug-drug interactions. The population and the cardiology ward were selected to initiate research on drug interactions in the hospital for convenience.

The prescribed medications were quantified and classified according to the Anatomical-Therapeutic-Chemical (ATC) Classification[13], up to the first level, which refers to the system where the medication acts.

The drug interactions of each patient were analyzed with the help of two software programs that check for drug interactions: Drugs.com[14] and Medscape[15]. Drugs.com[14] utilizes databases such as the American Society of Health-System Pharmacists, Cerner Multum, and IBM Watson Micromedex. It allows multiple drugs to be analyzed simultaneously, identifying potential interactions and classifying them as *"major," "moderate,"* or *"minor"* based on severity and clinical relevance. Medscape[15] maintains an independent, regularly updated database managed by a specialized editorial team. Its interaction checker also analyzes multiple drugs simultaneously, providing insights into interaction mechanisms, clinical significance, severity level, and management recommendations.

Drug interactions were categorized into four risk levels: (I) Contraindicated: High-risk interactions requiring medication replacement; (II) High Risk: Severe interactions where medication substitution should be considered; (Moderate Risk: Interactions where the benefits of treatment should be weighed against the potential risks; (IV) Low Risk: Interactions with minimal risk, where monitoring is recommended rather than medication changes.

Additionally, interactions were classified into pharmacokinetic interactions, which occur during drug (absorption, distribution, metabolism, or excretion), or Pharmacodynamic interactions, which involve drug-receptor interactions that either enhance or diminish the pharmacological effects. Each drug interaction was double-checked using both software tools to ensure accuracy.

All collected data was anonymized to protect patient confidentiality and was only analyzed following approval from the Research Ethics Committee (CEP). The study was approved under CAAE No. 22530919.0.0000.5071 through Opinion No. 3.838.864, issued on February 14, 2020.

Results

The admission (N=129) and discharge (N=127) prescriptions of 129 elderly patients hospitalized in the cardiology ward of a university hospital in Vitória, ES, Brazil, were analyzed. The average age of the patients was 71.8 years, as shown in Table 1. The gender distribution was relatively balanced, with 50.38% female and 46.62% male patients. The majority of patients (84.49%) identified as non-white (Black and mixed-race

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individuals). Additionally, most hospitalized elderly patients were married or in a relationship (48.83%). The majority resided in the Greater Vitória area (79.84%), and more than half of the patients (54.26%) did not report or were not asked about their educational background.

Table 1. Sociodemographic data of elderly patients admitted to the cardiology ward of a University Hospital.

	N	%
Total	129.00	100.00
Age		
< 70 years	62.00	48.06
70 years < x < 90 years	61.00	47.28
> 90 years	6.00	4.66
Sex		
Female	65.00	50.38
Male	64.00	49.62
Race		
White	16.00	12.40
No white	109.00	84.50
Not provided	4.00	3.10
Marital status		
With partner	63.00	48.83
Without partner	48.00	37.20
Other	18.00	13.97
Place of Birth		
Greater Vitória	103.00	79.84
Inland ES	21.00	16.28
Outside ES	2.00	1.55
Not provided	3.00	2.33
Education		
Incomplete primary school	17.00	13.17
Complete primary school	8.00	6.20
Incomplete secondary school	1.00	0.77
Complete secondary school	6.00	4.65
Not provided	70.00	54.26
None	23.00	17.82
Incomplete higher education	1.00	0.77
Higher education	3.00	2.36

The average length of hospital stay (considering only the first hospitalization per patient) was 14.09 ± 5.04 days. As seen in Table 2, the average number of medications prescribed per patient was 8.61 ± 3.07 at admission and 9.56 ± 3.18 at discharge. Polypharmacy prevalence in admission prescriptions was 89.14% (N=129), increasing to 92.12% (N=127) at discharge. The average number of potential drug interactions (PDIs) at admission was 6.95 ± 6.00 according to Medscape and 8.43 ± 7.34 according to Drugs.com. At discharge, the average number of PDIs increased to 8.27 ± 6.09 according to Medscape and 9.66 ± 6.97 according to Drugs.com.

Regarding ATC (Anatomical Therapeutic Chemical) classification at the first level, 10 out of 14 drug groups were identified in the study (Figure 1). The most frequently prescribed drug class (27.83%) was cardiovascular system medications (Class C).

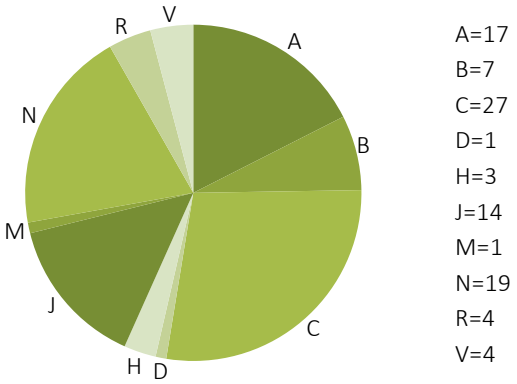
Table 2. Descriptive table of variables found in the medication prescriptions of elderly patients admitted to the cardiology ward of a university hospital

	Admission	Discharge
Average number of medications	8.61 ± 3.07	9.56 ± 3.18
Polypharmacy (%)	89.14	92.12
Average number of drug interactions		
Medscape[1]	6.95 ± 6.00	8.27 ± 6.09
Drugs.com[2]	8.43 ± 7.34	9.66 ± 6.97

[1]**Note:** https://www.medscape.com/.
[2]**Note:** https://www.drugs.com/.

The classification of PDIs is presented in Table 3. No contraindicated interactions were identified in either software. Moderate severity interactions were the most commonly observed. Additionally, a higher number of PDIs was found in discharge prescriptions across both software tools.

Figure 1. Classification at Level 1 of the Anatomical Therapeutic Chemical (ATC) classification of medications prescribed to elderly patients hospitalized in the cardiology ward of a university hospital, in absolute numbers, n = 97 (100.00%).



Note: A – Alimentary tract and metabolism: 17.00 (17.53%); B – Blood: 7.00 (7.22%); C – Cardiovascular system: 27.00 (27.84%); D – Dermatologicals: 1.00 (1.03%); H – Hormones: 3.00 (3.09%); J – Systemic antibiotics: 14.00 (14.43%); M – Anti-neoplastics and immunomodulators: 1.00 (1.03%); N – Nervous system: 19.00 (19.59%); R – Antiparasitic, insecticides, and repellents: 4.00 (4.12%); V – Various: 4.00 (4.12%); Total: 97.00 (100.00%).

Regarding the mechanism of PDIs, most interactions were classified as pharmacodynamic, both in Medscape (69%) and Drugs.com (89%).

The main potential drug interactions identified in the study are detailed in Table 4.

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Table 3. Classification of the severity of potential drug interactions found in admission and discharge prescriptions of elderly patients hospitalized in the cardiology ward of a university hospital.

Classification	Admission		Discharge	
Severity	**Medscape[1]**	**Drugs.com[2]**	**Medscape[1]**	**Drugs.com[2]**
Contraindicated	0	0	0	0
Severe	99	187	116	193
Moderate	776	760	929	904
Mild	209	76	87	227
Total	951	1.156	1.132	1.324

[1]**Note:** https://www.medscape.com/. [2]**Note:** https://www.drugs.com/.

Table 4. Frequency of the main potential drug interactions found in Drugs.com[15] in the prescriptions of elderly patients hospitalized in the cardiology ward of a university hospital and therapeutic alternatives.

Drug interactions	Classification	Frequency	Therapeutic alternative
Acetylsalicylic acid x Clopidogrel	Pharmacodynamics, moderate	141	Nonexistent, use with caution is recommended
Acetylsalicylic acid x Insulin human (regular)	Pharmacodynamics, moderate	114	Insulin dose adjustments may be necessary
Acetylsalicylic acid x Metoprolol succinate	Pharmacodynamics, moderate	100	No proposed clinical intervention
Acetylsalicylic acid x Enoxaparin	Pharmacodynamics, moderate	99	Nonexistent, use with caution is recommended
Enoxaparin x Clopidogrel	Pharmacodynamics, moderate	80	Nonexistent, use with caution is recommended
Acetylsalicylic acid x Losartan	Pharmacodynamics, moderate	71	Continuous monitoring, discontinue use or adjust NSAID dosage
Metoprolol succinate x Losartan[1]	Pharmacodynamics, moderate	62	Nonexistent, use with caution is recommended
Losartan x Insulin human (regular)	Pharmacodynamics, moderate	57	Insulin dose adjustments may be necessary
Acetylsalicylic acid x Glyceryl trinitrate	Pharmacodynamics, moderate	46	Monitor blood pressure near administrations
Acetylsalicylic acid x Furosemide	Pharmacodynamics, moderate	46	No proposed clinical intervention

[1]**Note:** https://www.medscape.com/. [2]**Note:** https://www.drugs.com/.

Discussion

The length of hospital stay observed in this study was similar to findings from previous research. Cuentro *et al.*[16], who analyzed the prevalence and factors associated with polypharmacy in elderly patients at a public hospital, reported a hospitalization period ranging from 1 to 103 days, with a mean of 21.07 days per patient. They found that hospital stays of 14 days or more were the most frequent, accounting for 50.9% of the sample.

Regarding the number of prescribed medications, Petri *et al.*[17] found a mean of 3.1 medications per patient (± 1.8) in hospitalized patients. The difference between their findings and the present study could be attributed to differences in study populations, as Petri et al. included patients aged 18 years and older, whereas the current study focused exclusively on elderly patients.

Polypharmacy in admission prescriptions showed higher values than those reported in other studies. Souza *et al.*[18] found that 63% of prescriptions for elderly patients treated at a specialty center presented polypharmacy. Cooper *et al.*[19] found that the interventions investigated in the review demonstrated benefits in reducing inappropriate prescriptions. However, they were unable to conclude on the outcomes of the interventions in clinically significant improvements such as the number of hospital admissions, ADEs, and overall quality of life of patients.

In a study on factors associated with drug interactions in hospitalized elderly patients, Veloso *et al.*[11] reported that 87.8% of patients experienced at least one drug interaction during hospitalization, with a median of four interactions per patient. However, their study did not account for multiple software tools for interaction detection. The present study identified an even higher number of interactions per patient, both at admission and discharge.

Terassi *et al.*[20] found the following distribution of medications in the prescriptions of institutionalized elderly patients, according to the ATC classification: the most consumed were those that act on the nervous system (class N, 36.48%), followed by medications that act on the cardiovascular system (class C, 23.17%) and, in third place, medications that act on the digestive system or alimentary tract and metabolism (class A, 22.94%). The present study found the same three main classes of prescription, but in the following order: medications that act on the cardiovascular system (class C, 27.34%), medications that act on the nervous system (class N, 19.59%) and medications that act on the digestive system or alimentary tract and metabolism (class A, 17.53%).

Sancar *et al.*[21], in a study on potential drug interactions in community pharmacy prescriptions, observed the following detection rates across three software tools: Medscape.com (33.3%), Drugs.com (31.3%), and Micromedexsolutions.com (21.2%). Significant differences were noted between the software, with Drugs.com detecting more interactions. However, moderate interactions

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were the most commonly identified across all platforms. These findings are consistent with the present study, which also found that moderate interactions were the most frequent.

The distribution of potential drug interactions (PIMs) by mechanism of action showed that most interactions were classified as pharmacodynamic, with 69% on Medscape and 89% on Drugs.com. This pattern aligns with Santos *et al.*[22], who analyzed elderly patients in a university hospital medical clinic and reported that 76.75% of interactions were pharmacodynamic, while 23.25% were pharmacokinetic, in a sample of 1,319 interactions. These results indicate a consistent trend across different clinical settings and databases, highlighting the complexity of drug effects on the body.

As shown in Table 4, the most frequent potential drug interaction was acetylsalicylic acid (aspirin) with clopidogrel, a combination of two drugs that modulate the coagulation system. Their concomitant use may lead to an increased risk of bleeding. It is important to note that aspirin, a nonsteroidal anti-inflammatory drug (NSAID), is commonly used at lower doses to prevent thrombotic events, especially in hospitalized patients with cardiovascular risk[23]. Carvalho[9], in a study on the prevalence of potential drug interactions in cardiology inpatients at a tertiary hospital, found 64 occurrences of aspirin-clopidogrel interactions, corresponding to 3.5% of the total 1,815 interactions identified. Additionally, interactions involving aspirin with enoxaparin or clopidogrel with enoxaparin also pose a considerable bleeding risk, requiring careful monitoring, especially when surgical intervention is necessary.

Another noteworthy interaction was between aspirin and regular human insulin, which can increase insulin's hypoglycemic effect, leading to hypoglycemia. Backes[10], in a dissertation on potential drug interactions in hospitalized patients, reported 67 occurrences of this interaction, which requires monitoring to prevent serious adverse events such as central nervous system depression and seizures. An additional PIM observed was between furosemide and aspirin, which can reduce the diuretic and antihypertensive effects of furosemide, potentially necessitating dose adjustments. Backes[10] also found 48 occurrences of this interaction in hospitalized patients.

Potential drug interactions in elderly patients with heart disease can be attributed to multiple factors: polypharmacy, characterized by the simultaneous use of multiple medications, is common in this population due to multiple comorbidities requiring distinct treatments; Physiological changes associated with aging, such as reduced renal and hepatic function, can alter drug pharmacokinetics and pharmacodynamics, increasing susceptibility to adverse interactions and Self-medication and the use of over-the-counter drugs without medical guidance also contribute to the risk of unwanted interactions[24].

The consequences of these interactions can be significant and varied. Synergistic interactions may lead to toxic effects, while antagonistic interactions can reduce the therapeutic efficacy of medications. For example, the combination of amiodarone and digoxin, commonly used in cardiac treatments, may result in cardiac toxicity and digitalis intoxication, respectively. Additionally, the concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) and certain antihypertensives may impair blood pressure control, increasing the risk of adverse cardiovascular events[12,24].

To mitigate these risks, it is essential to implement strategies such as medication reconciliation and pharmacotherapeutic follow-up. Medication reconciliation involves the systematic review of all medications the patient is using, especially during care transitions, to identify and resolve discrepancies. Continuous pharmacotherapeutic follow-up allows for monitoring the efficacy and safety of treatments, adjusting them as necessary to prevent harmful interactions. Studies indicate that these approaches can significantly reduce the occurrence of drug interactions and improve clinical outcomes in elderly patients with cardiac diseases[25].

This study presents some limitations that should be considered when interpreting the results. First, the sample was limited to a single university hospital, which may restrict the generalizability of the findings to other regions of the country and different healthcare settings. Additionally, the study was retrospective and based on prescription data, without direct evaluation of the clinical outcomes of the identified drug interactions. As a result, it was not possible to verify the occurrence of adverse events resulting from the interactions, reducing the ability to establish a causal inference between the detected interactions and their potential clinical impacts.

The clinical implications of the results are significant, as an increase in the average number of potential drug interactions at hospital discharge compared to admission was observed. This finding suggests the need for greater attention during care transitions across different levels of healthcare, reinforcing the importance of a thorough review of prescriptions and appropriate guidance for patients and caregivers. Strategies such as the implementation of medication reconciliation services and pharmacotherapeutic follow-up could mitigate risks associated with preventable drug interactions[26]. For future research, prospective studies are recommended to assess not only the presence of potential drug interactions but also their clinical outcomes, such as adverse drug events (ADEs), rehospitalizations, and morbidity and mortality.

Conclusion

Most patients included in the study had more than five prescribed medications (89.14% at admission and 92.12% at discharge), which may be associated with the increase in the number of potential drug interactions. The most commonly prescribed medications, according to ATC level I classification, were from classes C, A, and N, which act on the cardiovascular system, metabolism, and central nervous system. Among the potential drug interactions, the most frequent involved acetylsalicylic acid. This study contributes to the discussion on therapeutic alternatives, dose adjustments, and medication regimen optimization, paving the way for further investigations in other hospital wards and the establishment of best practices aimed at ensuring the safety of elderly patients, particularly in prospective studies.

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Contributors

PGR, SAGGJ, and BJPB - Project conception, data analysis, and interpretation of data; PGR, RAF, and BJPB- Article writing; SAGGJ, RAF, and BJPB- Critical review relevant to intellectual content.

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Conflict of Interest Statement

The authors declare no knowledge of any financial conflicts of interest or personal relationships that may have influenced the work reported in this article.

Artificial Intelligence (AI) Systems

No artificial intelligence systems were used.

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