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Factors associated with drug interactions in elderly hospitalized in high complexity hospital

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Abstract *This study aims to determine the frequency of potential drug-drug interactions (PDI) in hospitalized elderly and associated factors. This is a cross-sectional study in a teaching hospital. The dependent variable was the occurrence of potential drug interactions identified using DrugReax software. Patients with adverse drug reactions (ADR) related to clinical manifestations of PDIs were also identified. Multivariate logistic regressions was performed to analyze the association between the occurrence of PDIs and independent variables. In total, 237 older adults were included in the study. The prevalence of PDIs and interaction-related ADRs was 87.8% and 6.8%, respectively. The multivariate analysis showed a positive association between the detection of PDIs (OR 8.6; 95% CI, 2.5-30.0), and hospitalization due to a diagnosed circulatory system disease and number of medications > 14 (OR 9.8; 95% CI, 2.8-34.3%). The study showed a high prevalence of PDIs in the drug treatment of the elderly, but a lower prevalence of ADRs, as well as a positive association between PDIs and hospitalization due to a diagnosed circulatory system disease and number of medications > 14. The identification of factors associated with PDIs guides prevention measures for people that are more exposed to adverse events.*

Key words *Drug interactions, Adverse drug reactions, Aged, Drug therapy*

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Introduction

Aging carries an increased prevalence of chronic diseases and a higher number of medications[1]. Polypharmacy is common in elderly hospitalized patients and may lead to the use of potentially inappropriate medications for older adults, with a consequent increase in the occurrence of potential drug interactions and adverse drug reactions (ADR)[2]. These factors may reduce the safety of medication use, compromising the functionality of the elderly and also the efficacy of drug therapy[3].

Drug interaction is a clinical situation in which one drug can modify the action of another drug administered simultaneously or successively[4]. The probability of an individual having a drug interaction tends to increase with the number of drugs prescribed, number of therapeutic classes and age[2]. Medicines' use safety is ensured with the identification of drug interactions that may manifest clinically as ADRs and their potential risks[5].

Within this perspective, investigating potential drug interactions (PDI) during hospitalization is relevant because it contributes to the definition and development of strategies with the multidisciplinary team that can positively impact on the prevention and clinical management of these interactions and their negative outcomes in older adults. Therefore, this study mainly aims to determine the frequency of potential drug-drug interactions in the elderly during hospitalization and associated factors. A secondary objective identified patients with adverse drug reactions (ADR) related to the clinical manifestation of PDIs.

Methods

This is a cross-sectional study carried out in a 547-bed general public teaching hospital in Belo Horizonte, Minas Gerais, Brazil, providing medium and high complexity care.

For this purpose, non-probabilistic sampling was performed including all patients who met the following inclusion criteria: being elderly (aged 60 or over) hospitalized between January and December 2010 for a period ≥ five (5) days, in medical clinic wards of the investigated hospital. The list of inpatients in the study period in the medical clinic wards was obtained through the hospital census information system of the health institution investigated.

The documentary analysis was adopted for data collection and performed through a retrospective review of the selected medical records. We reviewed data of the medical records referring to the first hospitalization in 2010, analyzing the first day of hospitalization in the medical clinic until hospital discharge. The following documents or sections of the medical records were consulted to retrieve data: admission note, anamnesis, patient evolution, nursing observations, results of laboratory tests and medical prescriptions. Data were recorded in a previously prepared data collection instrument. Data on the demographic characteristics (gender, age), admission diagnosis, hospitalization time, health problems, number of medications, excessive polypharmacy (using 10 or more drugs, as per the concept suggested by Jyrkkä et al.[6] for use in studies of geriatric pharmacotherapy), occurrence of ADR and ADR-related drug interactions. All changes in the drug therapy of the patient during the hospitalization were recorded in the data collection instrument. Aspects of the development of the clinical history relevant to the investigation of ADRs were recorded.

The prevalence of drug interactions was identified by the Drug-Reax® software, Micromedex® database, and is available on the CAPES Journals[7] website. This database has adequate specificity and sensitivity for the identification of drug interactions in hospitalized patients[8-10].

Drug-drug interactions were classified regarding severity, adopting Drug-Reax® specifications: contraindicated (when drugs are contraindicated for concomitant use); major (when interaction may be life-threatening and requires immediate medical intervention); moderate (when the interaction may result in exacerbation of the patient's clinical condition or require a change of therapy)[7]. In this investigation, the interactions defined by Drug-Reax® as minor (when the interaction may have limited clinical effects without requiring changes in drug therapy) or unknown (when the level of severity is undefined)[7] were not included.

The dose of aspirinwas observed to identify the interactions involving this drug, since, for specific interactions involving acetylsalicylic acid, Drug-Reax® software informs, in the clinical management section, whether it occurs with doses used for analgesia and antipyresis (> 300 mg) or platelet antiaggregant effect (70-300 mg)[7].

We identified patients who developed ADRs as a result of the clinical manifestation of drug interactions to determine the prevalence of ADR

in the sample studied. Thus, we analyzed medication prescriptions, laboratory tests, nursing team annotations and clinical development records. The causality of the ADRs was verified using the Naranjo Algorithm, and those classified as dubious were not included in the study. The following definitions were adopted for the identification of ADRs:

Nephrotoxicity: 1.5 to 2-fold increased serum creatinine compared to the value before the onset of treatment or 0.3 mg/dL increase in absolute value within 48 hours of treatment. These parameters were based on the Acute Kidney Injury Network (AKIN) classification for the definition of acute kidney injury.

Hepatotoxicity: Five-fold elevation of alanine aminotransferase (ALT) or aspartate aminotransferase (AST) values against the upper limit reference value of the test or a twofold increase of the alkaline phosphatase and bilirubin test with the elevation of any value in AST or ALT against the upper limit reference value of the test.

- Hyponatremia: plasma electrolyte level below 135 mEq/L.
- Hyperkalemia: plasma electrolyte level greater than 5 mEq/L.
- Hypoglycemia: blood glucose below 70 mg/dL.
- Hyperglycemia: glycemia above 140 mg/dL (fasting) or 180 mg/dL (random collection).

For univariate and multivariate analysis, the occurrence of major or moderate potential drug interactions was defined as a dependent variable of the study. The independent variables selected were: gender, age (< 70 years, ≥ 70 years); length of hospital stay (≤ 12 days, > 12 days); number of health problems (≤ 3; > 3); diagnosis of circulatory system disease (yes vs. no); diagnosis of neoplasm (yes vs. no); number of drugs (≤ 14; > 14); and ADR related to drug interaction (yes vs. no). The quantitative variables (age, days of hospitalization, number of health problems, number of medications) were dichotomized by the median.

The information collected was entered into a database created in EpiData® software, version 3.1. Descriptive data analysis was performed by determining the frequencies and percentages of categorical variables and measures of central tendency (mean and median) and dispersion measures (standard deviation (SD) and interquartile range (IQR)) for quantitative variables.

The association between potential drug interactions and independent variables was performed using univariate analysis using the Pearson chi-square test. Fisher's exact test was used in the presence of at least one expected frequency below five (5).

The independent variables that obtained a value of $p \leq 0.25$ in the univariate analysis were included in the logistic regression model for multivariate analysis. The variables that maintained a value of $p < 0.05$ remained in the final model. Concerning univariate and multivariate analysis, the magnitude of the association was expressed by the odds ratio (OR) with 95% confidence interval (CI).

The likelihood ratio test was used to compare the models. The suitability of the final models was evaluated by the Hosmer and Lemeshow test. Statistical significance was considered when $p < 0.05$. Statistical analysis was performed in Statistical Package for Social Sciences® software (SPSS®), version 21.0.

The Research Ethics Committee of the Federal University of Minas Gerais (COEP-MG) approved the research project and was developed in compliance with all the ethical principles contained in Resolution Nº 466 of December 2012 on human research. The study was exempt from informed consent.

Results

The study sample comprised 237 older people, of which 120 (50.6%) were male. The median age was 70 years and the IQR was 13. The most prevalent admission diagnoses were diseases of the circulatory system (n = 95; 40.1%), neoplasms (n = 40; 16.9%) and respiratory system diseases (n = 36; 15.1%). The median number of health problems was 3 (IQR = 2).

The median number of medications used during hospitalization was 14, and 43.5% of patients (n = 103) used more than 14 medications during hospitalization and 78.1% (n = 185) had excessive polypharmacy (10 medications or more). A more detailed description of the studied population is described in Table 1.

Of the total number of elderly studied, 208 (87.8%) had at least one moderate potential drug interaction, with a total frequency of 1,288 interactions, with 394 different interactions. The maximum number of drug interactions per patient was 39 and the median was 4 (IQR = 9).

Regarding the severity of drug interactions, 1,102 (85.6%) were classified as moderate, 176 (13.7%) as major and 10 (0.7%) as contraindicated. The predominant mechanism of action of

the interactions studied was pharmacodynamic (n = 1,053; 81.7%), and pharmacokinetics (n = 147; 11.4) was the second most frequent. Regarding 5.4% (n = 69) of drug interactions, the mechanism of action was not elucidated and 1.5% (n = 19) of the drug interactions had a mixed action mechanism.

The most frequent serious interactions were aspirin + heparin (n = 46; 3.6%), clopidogrel + enoxaparin (n = 23; 1.8%), captopril + potassium chloride (n = 20; 1.6%) and clonazepam + morphine (n = 19; 1.5%). In the drug therapy of the 237 elderly patients, moderate interactions involving diuretic + angiotensin converting enzyme inhibitor prevailed: captopril + furosemide (n = 42; 3.3%), captopril + hydrochlorothiazide (n = 29; 2.2%), and enalapril + furosemide (n = 23; 1.8%). Other important moderate interactions detected in the elderly were: digoxin + furosemide (n = 25; 1.9%), carvedilol + digoxin (n = 18; 1.4%), captopril + spironolactone (n = 14; 1.1%), digoxin + simvastatin (n = 13; 1.0%) and losartan + spironolactone (n = 13; 1.0%) (Table 2).

The most frequent contraindications were citalopram + fluconazole (3), fluconazole + ondansetron (3), atazanavir + simvastatin (1) and cyclosporine + simvastatin (1).

Adverse drug reactions with probable or possible causality were detected in 50 (21.1%) of the elderly, and 62 ADRs were identified. We found that 34 (54.8%) of the ADRs could be related to drug interactions. Sixteen patients with ADR related to drug interactions were found, equivalent to 6.8% of the studied series. The ADRs related to drug interactions are shown in Table 3. Digitalis intoxication (16; 47.0%), hyperkalemia (5; 14.7%) and hypoglycemia (5; 14.7%) were the most frequent ADRs. The most frequent ADR-related interactions were digoxin + furosemide (4), digoxin + carvedilol (3), digoxin + spironolactone (3), spironolactone + losartan (2). Digoxin, spironolactone and insulin were the drugs most involved in interactions with clinical manifestation as ADRs.

In the univariate analysis, a statistically significant positive association between the occurrence of potential drug interactions and the following independent variables was identified: length of hospital stay greater than 12 days, number of health problems higher than three, number of medications prescribed greater than 14, diagnosis of disease of the circulatory system and neoplasm. In the multivariate analysis, the diagnosis of circulatory disease and number of medications higher than 14 were positively associated with drug interactions (OR = 8.6 and 9.8, respectively) (Table 4).

Table 1. Demographic Characteristics of the 237 Elderly in the Hospital investigated. Belo Horizonte (MG), Brazil, 2010.

Variable	Frequency	
	n	%
Patient		
Gender		
Male	120	*50,6*
Female	117	*49,4*
Age (years)		
> 70	115	*48,5*
≤ 70	122	*51,5*
Number of health problems		
≤ 3	156	*65,8*
> 3	81	*34,2*
Main hospitalization diagnoses		
Circulatory system disease	95	*40,1*
Neoplasms	40	*16,9*
Respiratory disease	36	*15,2*
Care		
Hospitalization time		
> 12 days	115	*48,5*
≤ 12 days	122	*51,5*
Drug Treatment		
Number of prescription drugs		
> 14	103	*43,5*
≤ 14	134	*56,5*
ADR[1] during hospitalization		
Yes	51	*21,5*
No	186	*78,5*
ADR-related drug interaction		
Yes	16	*6,8*
No	221	*93,2*

[1] ADR: Adverse Drug Reaction.

Discussion

The study detected a high frequency of potential drug interactions among hospitalized elderly. The hospital studied is of high complexity, which explains the frequency found, since it treats frail elderly patients with complex diseases and therapeutic regimens that require multiple medications. This care setting is an important determinant for drug interactions[11]. Prevalence of similar magnitude was detected in other investigations

Table 2. Major drug interactions with frequency greater than or equal to 10. Belo Horizonte (MG), Brazil, 2010.

Major drug interactions		Effect	Frequency
Drug 1	Drug 2		
Aspirin	Heparin	Increased risk of bleeding.	46
Clopidogrel	Enoxaparin	Increased risk of bleeding.	23
Captopril	Potassium chloride	Hyperkalemia.	20
Clonazepan	Morfine	Respiratory Depression.	19
Clopidogrel	Omeprazole	Reduced effect of clopidogrel and increased risk of thromboembolic events.	18
Digoxin	Spironolactone	Increased serum digoxin concentration.	18
Amlodipine	Simvastatin	Rhabdomyolysis.	16
Enoxaparin	Warfarin	Increased risk of bleeding.	15
Simvastatin	Warfarin	Increased risk of bleeding and risk of increased QT interval.	14
Clopidogrel	Heparin	Increased risk of bleeding.	13
Aspirin	Warfarin	Increased risk of bleeding.	11
Aspirin	Fluoxetine	Increased risk of bleeding.	10

involving elderly patients in a hospital setting, whose frequency ranged from 60 to 82.1%[4,11-14]. Concerning differences in study design, software used to identify interactions and clinical complexity of patients may be determinant of the variability between studies.

The drug interaction was positively associated with the number of medications and the diagnosis of circulatory disease in the elderly studied. The relationship between drug interaction and multiple drug use is widely described in the literature[4,11-15]. The drugs that work in the cardiovascular system were described as main drugs related to the occurrence of drug interactions in the elderly of the internal medicine unit[15]. The number of pathologies and length of hospital stay are essential predictors of drug interactions reported in the literature[4,12-16]. However, in the final logistic regression model of this study, these variables did not remain, possibly due to the high frequency in the casuistic, which hindered an adequate differentiation.

The frequency of ADRs resulting from the clinical manifestation of drug interactions, termed by some authors as actual interactions, was small. This result corroborates the prevalence of actual drug interactions detected in a prospective study developed with elderly hospitalized in Croatia, which was 9.5%, but including ADR and therapeutic inefficacy[4]. The prospective studies facilitate the display of the real interactions with higher reliability.

Interactions with clinical manifestations involving digoxin and other drugs were frequent in the casuistic investigated and are relevant in elderly care. Digoxin has a narrow therapeutic index, a factor that contributes to the increased risk of digitalis intoxication, and in the elderly, this risk is even more significant due to the pharmacokinetic changes that occur with aging, especially those related to renal elimination. The use of digoxin in geriatrics should be based on therapeutic clinical guidelines elaborated with scientific evidence and on the drug prescription criteria for the elderly to achieve adequate therapeutic results and avoid adverse events[17-19]. Monitoring serum levels of digoxin is essential, especially in the elderly, in order to ensure safety in the use of this drug[18].

It is also important to consider the clinical context of the elderly who usually have comorbidities and use multiple medications. However, it is typical for scientific studies and disease management guidelines not to provide specific approaches for patients with polypathologies and disregard the possibility of potential drug interactions[20]. The American Geriatric Society points out that the identification of drug-drug interactions is a critical element of streamlining the care of the elderly with polypathologies[21].

Hypoglycemia induced by drug interactions involved fluoroquinolones and beta blockers. In the study of drug interactions in older adults of a Mexican hospital, the interaction fluoroquino-

Table 3. Adverse Drug Reaction Frequency related to Drug-Drug Interaction. Belo Horizonte (MG), Brazil, 2010.

ADR	Drug interaction	ADR Frequency		Patients Frequency	
		n	%	N	%
Digitalis intoxication		**16**	**47.0**	**4**	**25.0**
	Digoxin x Furosemide	4			
	Digoxin x Carvedilol	3			
	Digoxin x Spironolactone	3			
	Digoxin x Captopril	2			
	Digoxin x Magnesium oxide	2			
	Digoxin x Alprazolam	1			
	Digoxin x Simvastatin	1			
Hyperkalemia		**5**	**14.7**	**3**	**18.7**
	Spironolactone x Losartan	2			
	Spironolactone x Cyclosporine	1			
	Spironolactone x Potassium chloride	1			
	Spironolactone x Enalapril	1			
Hypoglycemia		**5**	**14.7**	**3**	**18.7**
	NPH Insulin x Ciprofloxacin	2			
	NPH Insulin x Carvedilol	1			
	Regular Insulin x Ciprofloxacin	1			
	Regular Insulin x Propranolol	1			
Hematemesis		**2**	**5.8**	**1**	**6.3**
	Aspirin x Enoxaparin	1			
	Aspirin x Warfarin	1			
		2	**5.8**	**1**	**6.3**
Melena	Enoxaparin x Aspirin	1			
	Enoxaparin x Sertraline	1			
Hepatotoxicidade		**1**	**2.9**	**1**	**6.3**
	Pyrazinamide x Rifampicin	1			
Hyponatremia		**1**	**2.70**		
	Carbamazepine x Hydrochlorothiazide	1			
Hypotension		**1**	**2.9**	**1**	**6.3**
	Hydralazine x Furosemide	1			
Nausea		**1**	**2.9**	**1**	**6.3**
	Tramadol x Fluoxetine	1			
Fall		**1**	**2.9**	**1**	**6.3**
	Enalapril x Furosemide	1			
Total		34		16	

lones + insulin corresponded to 15% of the interactions, and was the most frequent. Adequate glycemic monitoring strategies and the dissemination of information on drug interactions that induce glycemia change are essential to ensure patient safety and prevent the damages resulting from these interactions[11].

Hyperkalemia is an important ADR that can be induced by drug interactions, exposing the patient to the risk of arrhythmias that can have serious consequences, especially in elderly individuals. Among the potential drug interactions that should be avoided in the elderly according to the 2015 version of the Beers criterion, we highlight interactions between potassium-sparing diuretics and angiotensin-converting enzyme inhibitors, whose clinical manifestation is hyperkalemia[17]. Hyperkalemia related to spironolactone in concomitant use with other drugs was frequent in this study. Frequent monitoring of serum po-

Table 4. Univariate and multivariate analysis of factors associated with potential drug interactions. Belo Horizonte (MG), Brazil, 2010.

Variable	Drug Interaction		Univariate Analysis		Multivariate Analysis[1]	
	Yes n (%)	No n (%)	OR (IC 95%)	p-value	OR (IC 95%)	p-value
Age						
> 70 years	98 (85.2)	17 (14.8)	0.63 (0.3 – 1.4)	0.245	----	----
≤ 70 years	110 (90.2)	12 (9.8)	1		----	----
Hospitalization time						
> 12 days	107 (93.0)	8 (7.0)	2.8 (1.2 – 6.6)	0.016	----	----
≤ 12 days	101 (82.8)	21(17.2)	1		----	----
Number of health problems						
> 3	77 (95.1)	4 (4.9)	3.7 (1.2 – 10.9)	0.02	----	----
≤ 3	131 (84.0)	25 (16.0)	1		----	-----
Health problems						
Circulatory system disease						
Yes	92 (96.8)	3 (3.2)	6.9 (2.0 – 23.4)	0.000	8.6 (2.5 – 30.0)	0.001
No	116 (81.7)	26 (18.3)	1		1	
Neoplasm						
Yes	32 (80.0)	8 (20.0)	0.4 (0.2-1.2)	0.000	----	----
No	176 (89.3)	21 (10.7)	1		----	-----
Number of prescription drugs						
> 14	100 (97.1)	3 (2.9)	8.0 (2.4 – 27.3)	0.000	9.8 (2.8 - 34.3)	0.000
≤ 14	108 (80.6)	26 (19.4)	1		1	

1: Hosmer-Lemeshow test: $\chi 2 = 3.48$; degrees of freedom = 6; p = 0.25 OR: Odds Ratio; CI: Confidence Interval.

tassium levels, especially in patients with chronic kidney disease, should be performed to identify this ADR[22].

The major enoxaparin-warfarin interaction is an example of drug interaction with a therapeutic goal. The concomitant use of warfarin with heparins in patients who are starting or restarting the use of this oral anticoagulant is desirable in the hospital setting in patients who have undergone a surgical procedure in which warfarin suspension is advocated[23]. Although the use of these drugs together is desirable in some situations, there is an increased risk of bleeding, especially in the elderly[7].

The aspirin + heparin and clopidogrel + enoxaparin interactions present an increased risk of bleeding, with the first being the most frequent interaction. In a Mexican hospital, these interactions were also frequent in prescriptions of the elderly[11]. The concomitant use of platelet antiaggregant with oral anticoagulants has benefits in acute coronary syndrome and as a secondary post-cerebrovascular accident prevention[24]. However, these drug combinations are associated with major adverse reactions[2], since older adults treated with antithrombotics are at increased risk of complications[16]. Frequent monitoring of signs and symptoms of bleeding is recommended.

The contraindicated interactions identified in the study have the potential to induce clinically relevant adverse events in elderly patients such as increased QT interval, myopathy and rhabdomyolysis. Concomitant administration of two or more drugs that prolong the QT interval may confer an additional risk for such prolongation and progression to Torsades de Pointes due to pharmacokinetic interactions that increase the plasma level of the drug that induces QT interval change or of a pharmacodynamic nature that potentiates the effect. Drug interaction is a significant risk factor for adverse events with drugs that alter the QT interval[25-27]. Thus, adequate evaluation and recognition of drug interactions that alter the QT interval are essential for the safety of drug therapy in this age group.

The enzymatic inhibition of the metabolism of citalopram by fluconazole can potentially induce serotoninergic syndrome, due to a pharmacokinetic interaction with probable occurrence in hospitalized elderly patients, classified

per severity as contraindicated. Although the serotoninergic syndrome is potentially fatal and rare, it is a predictable and preventable reaction, especially those related to drug interactions. Its frequency is increasing in recent years due to the widespread use of serotoninergic drugs in clinical practice[28].

Drug interactions involving simvastatin are clinically significant because they generally increase statin plasma levels as well as their potential to induce myopathies[29]. The interaction between amlodipine + simvastatin showed a high frequency in the drug therapy of the elderly studied, and pharmacokinetic studies evidenced an increased plasma concentration of simvastatin in the presence of this interaction[30-32]. Based on these studies, the Food and Drug Administration recommends that for the prevention of adverse events related to this interaction, the daily dose of simvastatin should be limited to 20 mg in clinical practice when in concomitant use with amlodipine. Another option to avoid this interaction is to prescribe therapeutic alternatives such as pravastatin or atorvastatin[32]. However, in the selection of the statin, besides considering its availability at the hospital, we should also evaluate its availability in extra-hospital care, noting whether it is affordable to the patient or if it can be got in the specialized component of pharmaceutical services to ensure continuity of use after discharge.

This study's limitations are the retrospective collection of data that can lead to bias in the analysis of ADRs due to the possibility of incomplete data in the medical records and because the design of the study does not allow us to establish a causal relationship. Also, only ADRs related to drug interactions were verified, and the lack of verification of therapeutic inefficacy may have underestimated the frequency of real interactions. The sample size and because the sample is non-probabilistic is another limitation of the study, restricting the generalization of the results. The logistic regression tends to overestimate the prevalence of high-occurrence events, such as potential drug interactions, and the odds ratio must be converted to a prevalence ratio using matrix calculations to interpret the data better. Poisson regression with robust variance is an appropriate alternative for use in cross-sectional studies, allowing the calculation of the prevalence ratio, avoiding overestimation of the association measures[33-36]. Despite the limitations of using logistic regression, this study shows that drug interactions in the drug therapy of hospitalized older adults are a frequent event in the hospital investigated and associated with the number of medications and the circulatory system diseases. Therefore, further research is required to understand better the magnitude of the problem among the elderly hospitalized in Brazilian hospitals.

On the other hand, the identification of associated factors may direct prioritization in the prevention of drug interactions and ADR. To this end, introducing the pharmacist in the follow-up of patients developing integrated activities with the health team is an essential contribution to greater safety in the use of drugs in hospitalized elderly individuals[14]. The clinical pharmacist, knowing the health conditions of the elderly and the characteristics of their drug therapy that predisposes them to the occurrence of DI, may establish criteria for the selection of older adults who should have this event monitored, seeking to avoid therapeutic failures or manifestation as ADR. Interactions involving high-alert medication should also be prioritized because they are associated with an increased risk of adverse events. Another contribution that optimizes the clinical results and the safety of the treatments is the suggestion of therapeutic alternatives that have no potential to induce DI. Also, the use of a computerized program for detecting potential drug interactions coupled with the hospital prescription system can be a tool to help the prescriber[13-15].

Conclusion

The study evidenced a high frequency of potential drug interactions among the elderly, but a reduced frequency of ADR due to clinical manifestations of interactions. Also, a positive association was detected between the occurrence of interactions and diagnosis by the diagnosis of circulatory disease and number of medications greater than 14.

Drug therapy in older adults should be prescribed with well-defined therapeutic objects and only when necessary. The number of medications used should be minimal to avoid adverse events from drug interactions. Drug interactions may be used for therapeutic purposes but may be associated with the risk of ADR. It is crucial to identify drug interactions that occur in the drug therapy of the elderly and implement measures to ensure treatment efficacy and safety. In this perspective, the identification of factors associated with drug interactions allows directing preventive measures to populations more exposed to the occurrence of adverse events.

Collaborations

RCSG Veloso contributed to the analysis and interpretation of data, drafting and relevant critical review of the paper's content, as well as being responsible for all aspects of the work of ensuring the accuracy and integrity of any part of the paper. MMG Nascimento contributed to the critical review and final approval of the version to be published. SCC Barroso contributed to the design of the project, the critical review and approval of the final version to be published. TP Figueiredo contributed to data collection and relevant critical review of the paper's content. AMM Reis contributed to the project design, data collection, analysis and interpretation, drafting and relevant critical review of the paper's content, and to follow-up on all steps of the work, ensuring the accuracy and integrity of any part of the paper.

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