

Risk of falls associated with drug therapy in hospitalized patients

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Abstract

The risk of falls and the administration of medications are related to the safety of hospitalized patients. Thus, this study aimed to identify classes of drugs and drug interactions that increase the risk of hospital falls. This was a quantitative, cross-sectional study, in the southern region of Brazil, with 612 patients from inpatient units. Data were collected using a specific instrument for demographic data, Morse Scale and medical chart analysis from June to August 2015. In the univariate statistical analysis, absolute and relative frequencies were used and in the bivariate analysis, a chi-squared test with a level of 5% significance was used. 612 patients participated in the study, with use of drugs that act on the cardiovascular and nervous systems prevailing. The main classes of drugs related to high risk of falls were antiparkinsonian (76.2%) and calcium channel blockers (57.1%). The number of medications was also associated with a high risk of falling, present in 56.2% of patients using five or more drugs. 2,187 drug interactions were identified, of which 9.1% were potentiating the risk of falls, among the drugs involved in serious or contraindicated interactions there was a higher frequency among patients taking morphine (16.5%) and metoclopramide (6.0%). The most frequent serious interaction was morphine and tramadol (7.7%). It was observed that drugs frequently used by hospitalized patients are associated with an increased risk of falls and that the existence of potential drug interactions also can increase the risk of falls. Knowing the profile of the drugs used and their relationship with the risk of falls in the hospital environment helps administrators implement preventive actions.

Palavras-chave: Accidents due to falls; Patient safety; Hospitalization; Medication.

INTRODUCTION

Falling is related to patient safety in the hospital environment and, in this sense, the World Health Organization, in 2004, launched the World Alliance for Patient Safety¹. In Brazil, in 2013, the Ministry of Health approved Ordinance N^o. 529, which instituted the National Patient Safety Program², composed of six goals, including the prevention of falls and the safe use

of medication.

An international study identified the variation in the rates of falls in hospitalized patients, with values from 1.03 to 4.18/1,000 patients/day³. In Brazil, studies report that the incidence of falls varies from 1.70 to 22/1,000 patients/day^{4,5}.

Currently, the identification of the risk of falls in the hospital environment can be performed by

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using scales, the one used in this study was the Morse Scale⁶. In addition to the items included in the said scale, the patient is also exposed to the use of medications that are identified as a factor that increases the risk of falls⁷. Research carried out in Canada demonstrated that 95.4% of hospitalized patients who suffered falls in general practice units used at least one medication associated with the occurrence of falls⁸. A study carried out in a teaching hospital in Belo Horizonte, MG found that 84.6% of patients used drugs that increase the risk of falling, especially drugs that act on the nervous system⁹.

Falls are influenced by intrinsic and/or extrinsic factors. Among the intrinsic ones is the use of medications, mainly hypnotics, hypotensive and sedatives¹⁰. Yet, research developed with the objective of assessing the risk of falls in hospitalized elderly people found that 45% of the sample had a high risk of falls identified by the Morse Scale and that diuretics had a significant association with the high risk of falls⁷.

A study that analyzed risk factors for falls, based on the diagnosis of the North American Nursing Diagnosis Association, identified that the continuous use of polypharmacy predisposes patients to adverse reactions and drug interactions and enhances this risk¹¹. Drug interaction is defined as the use of two or more drugs in such a way that the action or efficacy of one drug is significantly altered by the presence of another. Specifically, drug interactions represent a potential source of failures in care and risk for patients¹².

Patients with a potential risk of falling are those who have difficulty memorizing, muscle weakness and are over 60 years of age. In addition, polypharmacy is associated with the risk of falling and drug interactions can contribute to this occurrence¹³. Therefore, it is essential that health professionals know and monitor patients, the drugs prescribed and evaluate the drugs that potentially interact. These actions by health professionals aim to predict and minimize adverse events of the combined therapies, as the severity and possible effects of drug interactions

are related to clinical conditions, as well as the number and characteristics of the drugs consumed by patients¹⁴.

Given the above, studies indicate that drugs are intrinsic factors for the risk of falls^{15,16,17}. In this context, when considering drugs as fundamental in patient therapy, this study seeks to identify classes of drugs and drug interactions that increase the risk of falls for patients in the hospital.

MATERIALS AND METHODS

This is a cross-sectional, descriptive study, developed in three units of clinical and surgical admission at a private, size IV hospital in the southern region of Brazil. This institution provides 115 beds, of which 79 were part of the study. Patients admitted from June to August 2015 participated in the study.

The sample was defined with a margin of error of 3%, a 95% confidence level, a proportion of the risk of falling equal to 50% ($p=0.5$) and a population size of 1,356 hospitalized patients, in the same period of the previous year, which totaled 597 patients. To compensate for possible losses, a surplus of 5% was estimated, which produced 627 patients. Of these, eight refused, six were hospitalized more than once during the study, and one patient's data collection was incomplete, which resulted in 612 patients.

The inclusion criteria listed were patients over 18 years old, hospitalized in clinical or surgical units from June to August 2015, and interviewed within the first 24 hours of hospitalization. Exclusion criteria were patients who were admitted more than once during the study period.

Data collection was performed by the author and six nursing students, previously trained for the purpose of standardizing data collection. The collection included socio-demographic information, Morse Scale and analysis of medical

records. The search concerning medication occurred in the medical records and included all the drugs used by patients during hospitalization, regardless of route of administration, dose and pharmaceutical form.

The Morse Scale is used to assess the risk of falls and includes six topics: history of falls, secondary diagnosis, aids for walking, intravenous therapy/saline or heparinized intravenous device, gait and mental state⁶. Each topic has different scores between them. The classification occurs according to scores: from 0 to 24 points indicates a low risk of falling during hospitalization, between 25 and 44 is a moderate risk of falling, and 45 points or more high risk of falling⁶.

The choice of drugs classes that increase the risk of falling was based on previous studies that address the theme and included: cardiac therapy, antihypertensive drugs, diuretics, beta blocking agents, calcium channel blockers, agents at the level of the renin system -angiotensin, opioid analgesics, other analgesics and antipyretics, antiepileptics, psycholeptics, psychoanaleptics, antiparkinson drugs, constipation drugs and medications used for Diabetes Mellitus^{15,16}.

The organization of the medications was based on the Anatomical Therapeutic Chemical Classification System (ATC)¹⁸. In this study, the 1st and 2nd levels of ATC classification were used, and only for the evaluation of analgesics was the 3rd level used due to its fractional citation in the referenced framework¹⁸. To check the drug interactions that enhance the risk of falls, the Micromedex[®] software was used and were classified according to severity as: contraindicated, severe, moderate and mild. For the purposes of this study, drug interactions involving drugs that increase the risk of falls were considered exclusively, the effect of which is increased by drug interactions¹⁹. Medication not found in this database, such as dipyrrone, were researched in another source and their interactions were not classified; since this reference does not classify them in this study they were mentioned as yet to be evaluated²⁰.

Data analysis was performed using univariate and bivariate statistics. In the first, tables of absolute and relative frequency were used

to describe drug interactions. In the bivariate analysis, chi-squared test and Spearman's correlation coefficient were used. For all tests, a level of significance of 5% was considered in the R software. It should be noted that all ethical aspects recommended in the Regulatory Guidelines and Norms for Research Involving Humans were observed, in accordance with the National Health Council Resolution No. 466/2012. The study submitted and approved by the Research Ethics Committee, with CAAE 1.078.277 / 2015.

RESULTS

The characterization of the study participants is described in Table 1.

When assessing the relationship between medication use and risk of falls, it was found that most classes of drugs linked to the Cardiovascular System demonstrated an association with increased risk of falls. Among these, calcium channel blockers, beta blocking agents, diuretics, agents of the renin angiotensin system stand out. The majority of patients with a high risk of falls used cardiac therapy medications (60.0%), calcium channel blockers (57.2%) and beta blocking agents (56.3%) (Table 2).

Among the drugs that act on the Central Nervous System (CNS), the classes of antiparkinson (76.2%), psychoanalytic (51.3%) and antiepileptic (46.6%) drugs were associated with a high risk of falls. Among patients who used drugs for the digestive and metabolic tracts, those using hypoglycemic agents remained at a high risk (49.1%) of falls.

Regarding the number of classes of medication that increase the risk of falls, it was found that 56.2% of patients who used 5 or more classes of drugs had a high risk of falling (Table 3), with a significant difference between using less than 4 classes. Nine patients did not use any class, and of the total sample, the maximum used was 11 classes of medication

used concomitantly.

When ordinarily analyzing the risk of falls and the number of classes of medication, a significant association was observed ($p < 0.001$) and with $r = 0.351$ (data not shown).

In medical prescriptions, 2,187 drug interactions were identified, of which 9.1% (199) potentiate the risk of falls and 778 repeated. There was no interaction in their prescriptions for 29.1% (178) of the patients; in the other prescriptions, an average of 5 drug interactions were detected.

The drug interactions that increase the risk of falls were classified according to severity: severe (44.3%), moderate (39.2%), contraindicated (10.2%), risk to be assessed (4.6%) and mild (1.5%) (Table 4). The drugs most involved in serious and contraindicated drug interactions were morphine and metoclopramide. The most frequent serious interaction occurred between tramadol and morphine and with a contraindicated interaction between metoclopramide and citalopram.

The possible adverse events of the potential contraindicated interactions identified in the literature are related to extrapyramidal effects and among the serious ones, the event of strengthening the morphine effect and, consequently, respiratory depression.

Table 1 – Characterization of participants - Ijuí, RS, Brazil, 2015.

Variable		n	%
Age	18 to 60 years	342	55.9
	61 to 100 years	270	44.1
Sex	Female	381	62.3
	Male	231	37.7
Marital status	Not married	88	14.4
	Married	382	62.4
	Divorced	14	2.3
	Widower	82	13.4
	Separate	15	2.5
	Stable union	31	5.1
Education	Not literate	14	2.3
	Complete primary education	264	43.1
	Complete high school	137	22.4
	Complete Higher Education	168	27.5
	Postgraduate	29	4.7
Race	White	589	96.2
	Black	9	1.5
	Brown	14	2.3
Type of hospitalization	Surgical	324	52.9
	Clinical	288	47.1

Table 2 – Classes of drugs related to the classification of risk of falls on the Morse Scale of adult hospitalized patients - Ijuí, RS, Brazil, 2015.

Classes of Medication	Fall risk rating &			Total (%)	p
	0 - 24/ Low risk n(%)	25 - 44/ Moderate risk n(%)	≥ 45/ Risk high n(%)		
Cardiovascular system Cardiac therapy	1 (10.0)	3 (30.0)	6 (60.0)	10 (1.6)	0.081#
Antihypertensives REN ANG ^a System	42 (21.9)	73 (38.0)	77 (40.1)	192 (31.4)	<0.001
Diuretics	19 (17.0)	36 (32.1)	57 (50.9)	112 (18.3)	0.001
Beta blockers	14 (17.5)	21 (26.2)	45 (56.3)	80 (13.1)	<0.001
Calcium channel Block. ^b	2 (7.1)	10 (35.7)	16 (57.2)	28 (4.6)	0.001
Nervous system Pain relievers	198 (38.5)	155 (30.2)	161 (31.3)	514 (84.0)	0.895
Opioids	141 (43.8)	97 (30.1)	84 (26.1)	322 (52.6)	0.002
Psycholeptics	55 (27.5)	65 (32.5)	80 (40.0)	200 (32.7)	0.0003
Psychoanalytic	21 (17.6)	37 (31.1)	61 (51.3)	119 (19.4)	<0.001
Antiepileptics	27 (26.7)	27 (26.7)	47 (46.6)	101 (16.5)	0.001
Antiparkinson	1 (4.8)	4 (19.0)	16 (76.2)	21 (3.4)	<0.001
Digestive and metabolic tract Constipation Drugs	24 (33.8)	17 (23.9)	30 (42.3)	71 (11.6)	0.120
Hypoglycemic	9 (15.8)	20 (35.1)	28 (49.1)	57 (9.3)	0.001

^a0% within each drug class; % within the system; p for the chi-square test; #p likelihood ratio test; ^aRenin-angiotensin system = REN ANG; ^b Calcium channel blocking agents = Calcium channel Block.

Table 3 – Number of classes of medication, which increase the risk of falls, used by patients associated with the risk of falling - Ijuí, RS, Brazil, 2015.

Number of medication classes the patient uses	Classification of Risk			Total (%)	p
	0 - 24/ Low Risk n (%)	25 - 44/ Moderate risk n (%)	≥ 45/ High risk n (%)		
Up to 4	210 (43.6)	147 (30.5)	125 (25.9)	482 (80.0)	<0.001
5 or more	17 (14.0)	36 (29.8)	68 (56.2)	121 (20.0)	

Source: Research data, 2015.

p for the chi-square test; 9 patients did not use medication and were not part of this analysis

Table 4 – Drug interactions that increase the risk of falling - Ijuí, RS, Brazil, 2015.

Efeito		Drug Interaction		
Medicine 1	Medicine 2	Número de ocorrências	% ^{&}	Gravidade da Interação
Respiratory depression				
Tramadol	Morphine	47	7.7	Serious
Captopril	Morphine	35	5.7	Serious
Diazepam	Morphine	19	3.1	Serious
CNS depression				
Diazepam	Omeprazole	37	6.0	Light
Alprazolam	Omeprazole	17	2.7	Moderate
Carbamazepina	Omeprazole	14	2.3	Moderate
Hypotension				
Enalapril	Furosemide	16	2.6	Moderate
Captopril	Losartana	12	2.0	Serious
Captopril	Furosemide	10	1.6	Moderate
Hypoglycemia				
Regular Human Insulin	Metformin	12	2.0	Moderate
Enalapril	Metformin	11	1.8	Moderate
Captopril	Metformin	9	1.5	Moderate
Extrapyramidal effect				
Metoclopramide	Citalopram	18	3.0	Contraindicated
Metoclopramide	Amitriptyline	9	1.5	Contraindicated
Metoclopramide	Chlorpromazine	9	1.5	Contraindicated
Convulsion				
Cyclobenzaprine	Morphine	18	3.0	Serious
Dipyron	Levofloxacin	9	1.5	Risk to be assessed
Paroxetine	Tramadol	5	0.8	Serious
Rabdomiólise				
Risperidona	Simvastatin	2	0,3	Serious
Varfarina	Simvastatin	2	0,3	Serious
Cetoconazol	Simvastatin	1	0,2	Contraindicated

Source: Research data, 2015.

[&]percentage in relation to the number of patients in the study (n=612)

DISCUSSION

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In this study, it became evident that the use of drugs that act on the cardiovascular and nervous systems are associated with an increased risk of falls, as well as the presence of drug interactions. These results corroborate with the systematic review²¹ that identified among the drugs associated with the occurrence of falls those that act on the cardiovascular and nervous system. Moreover, the results verified in a hospital linked to the Unified Health System in Belo Horizonte, MG, also identified these two classes of drugs as the most frequent among drugs that increase the risk of falling. In a total of 284 drugs 57.3% were drugs of the central nervous system and 42.7% of the cardiovascular system⁹.

It was found that all antihypertensive drugs used by patients were related to the high risk of falling. Medication used for the cardiovascular system were mentioned in a study related to the risk of falls^{15,21}. Attention that must be given to these drugs includes the occurrence of hypotension, muscle weakness and urinary urgency¹⁶.

In national studies, among antihypertensive drugs, the use of diuretics with the risk of falling is highlighted. In a hospital in Rio de Janeiro, postural hypotension was identified in the surgical clinic as a risk factor for fall present in 34.7% of patients, and observed that a patient who had a fallen during the study used diuretic medication and had symptoms of postural hypotension and dizziness¹⁶. In a university hospital in Paraíba, it was also shown that patients who used antihypertensive drugs (29.2%) and diuretics (16.9%) were also at a high risk of falling⁷. The authors present that in addition to the symptoms of fatigue, hydroelectrolytic disorders and postural hypotension, the use of these drugs increases the frequency for urination, causing patients to move around frequently, increasing their risk of falls and fractures⁷.

Of the drugs that act in the CNS, antiparkinson agents, psycholeptics, psychoanaleptics and antiepileptics were related to the high risk of falls. This association stems from the potential adverse effects of drugs that act on the nervous system, which include drowsiness, dizziness, weakness and gait disorders, which can potentiate the occurrence of falls²¹. A study carried out in Pennsylvania with the aim of analyzing the association between medication dosage in the CNS and the risk of serious falls, including hip fractures, in individuals with a history of falls concluded that older patients with a history of falls or fractures of the hip were more likely to have another severe fall than those who did not take any CNS medication²².

Moreover, research aiming to explore the association between medications and risk of falling in hospitalized patients suggested that patients who use psychotropic medications in their treatment (antidepressants and/or opioid analgesics) should be monitored for the risk of falling daily, in the first three days of use¹³. A cohort study carried out in the United Kingdom with the aim of providing a comprehensive risk assessment by class of drugs for the most commonly prescribed antidepressants followed 238,963 patients diagnosed with depression, and of these, 4,651 patients suffered a fall²³. Over five years, falls and fractures have been reported, and all classes of antidepressant drugs have been associated with significantly high rates of falling²³.

Psychoanaleptics alter cognitive functions such as attention, memory, drowsiness and orientation, which are important for balance control. In this perspective, it is necessary for the interdisciplinary team to plan for differentiated care given to patients who use these medications. This may be through the execution of preventive actions in groups of

evaluated medical prescriptions, planning standardized schedules for medication administration, knowing the profile of the medications used and their potential risks, as well as paying attention to the physical support structure for the patient's walking, the furniture and lighting of the room.

Regarding the use of hypoglycemic agents, patients were associated with a high and moderate risk of falls. Corroborating this result, a study mentioned that prescribed oral antidiabetics increase falling by three-fold as a result of the hypoglycemic effect¹³. Another study reported that patients who experienced hypoglycemic episodes were more likely to have fractures related to falls than those who did not have such an adverse event²¹.

In the present study, patients used an average of two to five classes of drugs and these results are similar to other studies^{13,24}. Polypharmacy also appeared as a factor associated with a high risk of falling, since more than 50% of patients using five or more medications were at a higher risk, which is in line with the literature in a study that identified among the factors linked to falls the use of five or more medications²⁵. Still, there was a low correlation between the risk of falls and the number of classes of drugs used. Although the number of classes did not interfere in the classification of the risk of falling, the particularities of each class of drugs and the interactions between them can potentiate it.

In this sense, a study carried out in Taiwan confirmed the association between polypharmacy and the increased risk of fractures related to falling. The authors suggest that to reduce this clinical incidence, researchers should consider and identify inappropriate prescriptions²⁶. Research with the objective of evaluating the degree of reproducibility of the Morse Scale in a hospital context and analyzing its validity through correlations with other measurement instruments, found that 30.0% (60) of the

patients were medicated with two drugs and 27.5% (55) with a drug associated with the risk of falling²⁷. This finding proves the need to assess the use of medications and the Morse Scale in association with identifying the risk of falling. Although the simultaneous use of multiple medications can often increase therapeutic efficacy, certain combinations can incur harm to the patient²⁸.

Therefore, the present study identified 2,187 potential drug interactions between the drugs used by patients, of which 9.1% were considered to increase the risk of falls due to their potential adverse effects. Among the interactions, 37 were classified as contraindicated, which should be avoided because their risks outweigh the benefits, represented mainly by the combination of metoclopramide and citalopram that increase the risk of extrapyramidal reactions.

Amid the common adverse effects related to various medications, symptoms of extrapyramidal reactions are among the most frequent and severe related to the risk of falling. Motor activity is regulated by the extrapyramidal system and modulated by neurotransmitters; thus, the most common adverse effects are dystonic reactions that are characterized by muscle contractions that produce repetitive torsional movements, spasms or abnormal postures²⁸.

The interaction between tramadol and morphine was the most frequent among the serious interactions. The effect of the association of these two drugs can result in respiratory depression, which increases the possibility of falling²⁹. A study demonstrated that patients with tramadol prescription should have their risk of falling assessed daily¹³. This study identified only the potential drug interactions and did not follow the manifestation and outcome of these effects during hospitalization, such as the manifestation of a drug interaction and the event of falling, which is a limitation of the

study.

Although not all drug interactions can be prevented, it is necessary that permanent education be promoted among health professionals, including the nursing team that provides comprehensive patient care, with an emphasis on risk factors for drug interactions and pharmaceutical classes³⁰. A study found that knowledge about the risk factors associated with medications can contribute to prevention and even reduce falls. The study also found that the constant evaluation of all health professionals is important for the implementation of prevention strategies, not only related to the use of medications, but education for the self-care and physical structure of the institution¹⁶. It is necessary to identify the patient and monitor him differently by a team working on the medical prescription process. This process involves the doctor in the prescription, the nurse in the schedule, the pharmacist who reviews it, the pharmacy assistants who dispense them and, again, the

nurse that finishes with the administration of the medication to the patient. During all these stages the patient remains under the care of the team and the family. It is necessary to consider the role of each professional involved in the administration of medications. The role of ensuring safe care is that of all professionals, including the family and the patient.

This stems from the fact that drug interactions and the number of classes of drugs can influence the physiological effects of this association and increase the risk of falls. In addition, these effects involved the safety of hospital patients and the discussion of actions that minimize their exposure to adverse events.

This study had some limitations because it was a cross-sectional study and, thus, does not establish a temporal relationship with the studied population. Therefore, longitudinal studies could improve the understanding of the relationship between drug classes and the risk of falls in the hospital environment.

CONCLUSION

This study showed that there are classes of drugs, especially those that act on the cardiovascular and nervous systems that enhance the risk of falling, as well as the use of polypharmacy and the potential drug interactions also were related to the risk of hospital falls. These results associated with the classification of patients by the Morse Scale made it possible to identify in the hospital environment the patients most susceptible to falls due to their therapeutic plan and risk factors.

Based on these results, it is possible to

propose, in the hospital environment, the creation of protocols for monitoring patients at higher risk of falls and their associated factors, such as the use of medications and their potential interactions, in order to reduce their risk and promote patient safety, as well as the maintenance of their functional capacities and autonomy. For this, the need for training and instrumentalization of all health professionals involved in care is highlighted, in order to avoid prescription and drug interactions, as well as to identify the occurrence of adverse effects that may influence the patient's health.

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