Drug scheduling by nurses and drug interactions in patients with cardiovascular diseases

O agendamento de medicamentos pelo enfermeiro e as interações medicamentosas em pacientes com doenças cardiovasculares

Programa de enfermería de medicamentos e interacciones con drogas en pacientes con enfermedades cardiovasculares

Natália da Palma Sobrinho[I]
ORCID: 0000-0003-3187-2832

Juliana Faria Campos[I]
ORCID: 0000-0001-7254-5251

Rafael Celestino da Silva[I]
ORCID: 0000-0002-5211-9586

[I]*Universidade Federal do Rio de Janeiro. Rio de Janeiro, Rio de Janeiro, Brazil.*

Corresponding author:
Rafael Celestino da Silva
E-mail: rafaenfer@yahoo.com.br

ABSTRACT

Objectives: to identify and characterize the potential serious drug interactions in patients hospitalized with cardiovascular diseases, relating them to the schedules established for drug administration by nurses. **Methods:** a documentary, quantitative and sectional research. Ninety-nine prescriptions from patients admitted to the cardiology ward of a hospital in Rio de Janeiro for more than 48 hours were analyzed. Drug interaction was assessed using the Micromedex® software. The data were analyzed using descriptive and inferential statistics. **Results:** serious interactions were evidenced in 22 drug pairs, most frequently at 6 p.m. and 6 a.m., times with higher dose scheduling performed by nurses. The most recurrent drug pairs involved in serious interactions were simvastatin + amlodipine and enoxaparin + clopidogrel. **Conclusions:** drug scheduling by nurses requires a review of the criteria for proposing schedules for drugs in order to ensure patient safety.
Descriptors: Drug Prescriptions; Drug Interactions; Patient Safety; Cardiology; Nurses.

RESUMO

Objetivos: identificar e caracterizar as potenciais interações medicamentosas graves em pacientes hospitalizados com eventos cardiovasculares, relacionando-as com os horários estabelecidos para administração de medicamentos pelo enfermeiro. **Métodos**: pesquisa documental, quantitativa e seccional. Foram analisadas 99 prescrições de pacientes internados na enfermaria cardiológica de um hospital do Rio de Janeiro há mais de 48 horas. As interações medicamentosas foram avaliadas pelo *software* Micromedex®. Esses dados foram analisados por estatística descritiva e inferencial. **Resultados**: evidenciaram-se interações graves em 22 pares medicamentosos, com maior frequência às 18 horas e 06 horas da manhã, horários com maior agendamento de doses realizado pelos enfermeiros. Os pares de medicamentos mais recorrentes envolvidos nas interações graves foram sinvastatina + anlodipino e enoxaparina + clopidogrel. **Conclus**ões: o agendamento de medicamentos pelo enfermeiro demanda revisão dos critérios para a proposição de horários para os medicamentos em vista da garantia da segurança do paciente.
Descritores: Prescrições de Medicamentos; Interações de Medicamentos; Segurança do Paciente; Cardiologia; Enfermeiras e Enfermeiros.

RESUMEN

Objetivos: identificar y caracterizar las posibles interacciones medicamentosas graves en pacientes hospitalizados con eventos cardiovasculares, relacionándolos con los horarios establecidos para la administración de medicamentos por parte de la enfermera. **Métodos:** investigación documental, cuantitativa y seccional. Se analizaron 99 recetas de pacientes ingresados en la sala de cardiología de un hospital en Río de Janeiro durante más de 48 horas. Las interacciones farmacológicas se evaluaron utilizando el software Micromedex®. Estos datos se analizaron mediante estadística descriptiva e inferencial. **Resultados**: se evidenciaron interacciones graves en 22 pares de fármacos, con mayor frecuencia a las 6 p.m. y a las 6 a.m., veces con una programación de dosis más alta realizada por las enfermeras. Los pares de fármacos más recurrentes involucrados en interacciones graves fueron simvastatina + anlodipino y enoxaparina + clopidogrel. **Conclusiones:** la programación de medicamentos por parte de las enfermeras exige una revisión de los criterios para proponer horarios de medicamentos con el fin de garantizar la seguridad del paciente.
Descriptores: Prescripciones de Medicamentos; Interacciones de Drogas; Seguridad del Paciente; Cardiología; Enfermeros

INTRODUCTION

Drug interaction is an expressive incident that can occur along the path of the drug system. Its duration may represent an error in the use of drugs. It is defined as the change in pharmacological effects between two or more concomitant drugs administered, which may result in an increase or decrease in therapeutic efficacy or in adverse events caused by such effects, or even in the emergence of new effects[1].

Regarding severity, interactions are classified as: mild, in general, does not require a major change in therapy; moderate, the interaction may result in an exacerbation of the patient's condition and/or require a change in therapy; and severe, interaction can be life-threatening or require medical intervention to minimize or avoid serious adverse effects[2].

Some drug interactions are beneficial, as they aim to treat diseases by increasing the therapeutic efficacy obtained by combining substances that act in more than one stage of the mechanism of action. This association can also improve treatment adherence, due to the lower number of doses to be ingested, and reduce toxic effects[1].

In the case of the article in question, the interest is the drug-drug interactions that change the drug's biochemical or physiological effect (pharmacodynamics)[1]. The interactions are considered undesirable and unnecessary, since they can lead to ineffective therapy, increased time and cost of hospitalization and even serious events that compromise the patient's life[3]. In particular, serious interactions related to drug therapy used in patients with cardiovascular diseases.

Such diseases have high rates of morbidity/mortality, accounting for 29.8% of the total number of deaths and being considered the main cause of death in the country. Among them are ischemic, cerebrovascular, hypertensive diseases and congestive heart failure[4]. The latter is responsible for a high in-hospital mortality rate that places Brazil in a prominent position[5]. It should be added that the increased involvement by cardiological morbidities is also explained by the population aging profile, which brings together the higher prevalence of chronic non-communicable diseases, such as hypertension[4].

In the care of patients with cardiovascular diseases, drug therapy is essential for better control of their clinical condition. Thus, individuals are often susceptible to the use of several drugs in the context of complex therapeutic regimens, which warns of the concomitant use of cardiovascular drugs and the possibility of drug interactions in this clientele[3,6].

This is because polypharmacy is one of the main risk factors for drug interactions. Polypharmacy is defined as the use of many drugs (five or more). It is associated with increased risk and severity of adverse reactions, precipitating drug interactions, causing cumulative toxicity and increasing morbidity, and mortality[7].

The studies already developed in the cardiological area indicate a high percentage of interactions. An example of this is research with hypertensive elderly people, in which the occurrence of drug-drug interactions was high in patients who used an average of seven drugs. Among the serious interactions, amlodipine and simvastine stood out, due to the risk of rhabdomyolysis[8].

In the investigation of the prevalence and types of interactions in 2,342 cardiac patients admitted to a Pakistani hospital, 91.6% of the patients had at least one interaction. Among the 5,109 potential drug interactions presented, 55% were classified as moderate and 45% as more severe[9].

This production of knowledge about drug interactions in the specificity of cardiology shows that most studies are carried out at ICU's, mainly by doctors and pharmacists, without establishing links with the scheduling performed by nurses[10-12]. This last aspect is relevant, since the polypharmacy characteristic of the therapy of patients with cardiovascular diseases impacts on nurses' practice of scheduling the times for the administration of drugs prescribed by the doctor.

In this regard, it can be seen in the literature that there are risks to patient safety related to scheduling, especially the occurrence of drug interactions[13-15]. In a research that described the drug management prescription by nursing in a surgical clinic, the use of pre-defined schedules in the schemes was evidenced: 4/4 hours, 6/6 hours, 8/8 hours, 12/12 hours, which increased the risk of interaction among drugs in prescriptions with polypharmacy[13].

Another investigation on scheduling non-conformities in 362 general Intensive Care Unit (ICU) prescriptions showed a high frequency of scheduling with intervals not consistent with the prescription, increasing the possibility of interactions[14].

A study that analyzed potential serious interactions resulting from the scheduling of intravenous drugs found 43 serious interactions in 135 prescriptions analyzed. For the authors, nurses still perform this activity in most hospitals, following a fixed schedule routine that rarely considers drug characteristics and/or the patient's clinical condition, favoring drug interactions[15].

Considering the experience of the researcher acting as a nurse in a cardiac inpatient unit, there was a lack of use of criteria for scheduling drug administering. Nurses were guided by a fixed schedule routine, without considering the pharmacological groups, their mechanisms of action and potential drug interactions (PDI), the study proposal to analyze the scheduling relationships with the occurrence of drug interactions is justified.

Its relevance is in line with the initiatives of the World Health Organization, which introduced in 2017 the document called Patient Safety Challenge on Medication Safety. This document aimed to reduce by 50% the serious and preventable damage associated with drugs in the next five years[16]. Furthermore, it should be noted that the safety protocol for the prescription, use and administration of drugs is an integral part of the goals of the Brazilian National Patient Safety Program (*Programa Nacional de Segurança do Paciente*). This program aims to promote safe practices and prevent adverse events related to drugs[17]. Within this protocol, the approach to drug interactions and their outcomes is still incipient, so the knowledge produced may contribute to its improvement.

OBJECTIVES

To identify and characterize the serious PDI in patients hospitalized with cardiovascular diseases, relating them to the schedules established for drug administration by nurses.

METHODS

Ethical aspects

Regarding the ethical aspects, the study was approved by the Research Ethics Committee, CAAE (*Certificado de Apresentação para Apreciação Ética* -Certificate of Presentation for Ethical Consideration) 56849816.4.0000.5238, under Opinion 1612961. As this is a research with secondary data, signing the Informed Consent Term was waived.

Study design, period and location

This is a documentary, exploratory, quantitative and sectional cut research, developed with the support of the STROBE tool. It was performed from August to September 2016 in the cardiology inpatient unit of a hospital in Rio de Janeiro that has 30 beds for admission. This is a reference institution for procedures of medium and high complexity that are part of the Sentinel Surveillance System.

In the investigated setting, drug system is computerized through institutional software, and begins with the selection of the drug for prescription by the doctor. Then, there is the choice of times for drug administration by nurses, also through this electronic system, mandatory step for the prescription to be released to the pharmacy in the morning. It is noteworthy that in such an electronic system there is no resource for sending automatic alerts regarding the risk of drug interactions from the scheduling of schedules performed by nurses, leaving the professional to analyze its adequacy.

The pharmacy sector receives order and the clinical pharmacist carries out a prior evaluation of the prescriptions and, if deemed necessary, contacts the doctor and/or nurse for clarifications and/or suggestions. This role of the pharmacist gives the possibility of analyzing prescription errors and scheduling. From this validation of the prescription, drugs are separated into unit doses and sent to the sectors with the printed prescription in the early afternoon (until 2 p.m.), with the provision of drugs for the period of 24 hours. The nursing team is responsible for receiving these drugs, checking, preparing and administering them to patients, in addition to recording and monitoring their reactions. There is no satellite stock in the sectors.

Sample, inclusion and exclusion criteria

The research sample was determined using the sample calculation formula for finite populations, taking into account a 95% confidence level, a sampling error margin of 0.05 (p=0.05) and universe of eligible prescriptions (quantity average number of prescriptions performed per month at the chosen clinic). This universe was determined based on the average number of patients admitted to the cardiology ward and the average number of days of hospitalization, which resulted in an average amount of 160 prescriptions/month. The percentage of 20% of PDI caused by nurses' scheduling was admitted, based on the literature[18].

After applying the formula, the sample established was 99 prescriptions. Given this amount, drug prescriptions of patients hospitalized with cardiovascular diseases in the unit that met the criteria were investigated: over 18 years of age, in pharmacological therapy with at least two prescription drugs and hospital stay longer than 48 hours.

The retrospective time frame established for the analysis of the patients' medical records to capture the prescriptions was for April, May and June, 2014. It was based on the multidisciplinary team agreement that works in the institution that, in this period of the year, hospital care does not suffer seasonal influence, therefore, without influences on the profile of patients with cardiovascular diseases and the main drugs used.

Furthermore, a single prescription was chosen for analysis, referring to 48 hours of hospitalization. This is because, in the first 24 hours, prescription tends to be performed by a non-specialist professional in the sector where this patient was admitted, such as emergency. Thus, in this period there is still the possibility of insertion and adjustment of drugs, which could bring some information bias to the study. Therefore, it was understood that in the 48 hours of hospitalization, the prescription was already performed by a cardiologist and composed of the necessary drugs to achieve the planned therapeutic results, which justifies his choice.

Study protocol

Based on the inclusion criteria, 140 prescriptions were eligible to be included in the research, which were numbered sequentially and then random numbers were drawn until reaching the total of the study sample, that is, 99 prescriptions. For data collection, a structured instrument was used, consisting of: sociodemographic variables; variables on clinical aspects, such as main medical diagnoses, outcome of hospitalization; drugs prescribed and schedule proposed by nurses for drug administration. It was decided to collect this data from the profile of the clientele served in order to establish links with the prescribed drugs and the clinical repercussions during the PID.

To assess drug interactions, the Micromedex® software was used, which identifies PDI's and classifies them. Access was through the website "https://intranet.ufrj.br/inicio/periodicos", followed by a search engine for the Micromedex® software. When accessing Micromedex®, the drug interaction tab was selected and the drugs were submitted to the software using the generic name, according to the drug prescription. Drugs were subjected to analysis grouped by pairs based on the scheduling performed by nurses.

Based on this, the program classified PDI's according to severity (mild, moderate and severe), clinical evidence (reasonable, good and excellent documentation) and presented clinical repercussions. As for documentation, the software classified interactions as excellent, when controlled studies consistently demonstrated the interaction; good, which strongly states the interaction, but there is a lack of controlled studies; and reasonable, at which the studies are unsatisfactory, but the pharmacological aspects sufficient to affirm the occurrence of the interaction.

Analysis of results and statistics

For the organization of the data and its statistical analysis, the Excel® software was used. In the characterization data,

the discrete variables were analyzed using the descriptive statistical measures of absolute and relative frequency and the continuous ones, using the central tendency measures. For the analysis of potential drug interactions, descriptive statistical measures were calculated as absolute and relative frequency. Bivariate analysis was used to assess the occurrence of severe PDI according to the drug scheduling times. *Odds Ratio* was calculated with the aid of the MedCalc software to obtain the chance of occurrence of potential drug interactions in prescriptions that had 5 drugs or more prescribed, considering the significance level of p ≤0.05.
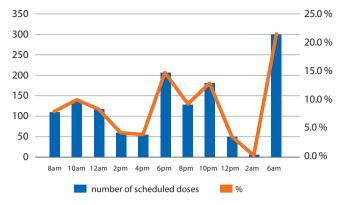
RESULTS

As for the demographic and clinical profile of patients with cardiovascular diseases admitted to the clinic studied, of the 99 prescriptions selected, 59% referred to male patients and 41% female, with a mean age of 71.7 (± 15.1) years. Regarding females, the average was 75.8 years and for males 67.2 years. The most prevalent medical diagnoses according to the ICD-10 were congestive heart failure (22.2%) and acute myocardial infarction (20%). Males were more affected by heart failure and acute myocardial infarction, while females were affected by angina and arrhythmias. The outcome of hospitalization was 91.9% for hospital discharge and 8% death.

In the profile of the drug scheduling performed by nurses, 366 scheduled drug doses were identified, as well as 24 prescribed drug classes, the main ones being the antihypertensive drugs with 133 doses (13.89%), the analgesics with 116 doses (12.07%), diuretics with 70 doses (7.28%) and antiplatelet agents with 46 doses (4.78%). 696 (51%) doses were scheduled for the day service and 670 (49%) for the night service.

The highest number of scheduled doses, considering the schedules individually, occurred at 6 a.m. with 301 doses, followed by the 6 p.m. schedule with 208 doses, as shown in Figure 1. It is noteworthy that among the three most prevalent hours, two were hours of responsibility for night service (10 p.m. and 6 a.m.).

From the analysis of the scheduled pairs made by Micromedex, 57 PDI's were identified, present in 51 prescriptions, classified as mild 5 (8.77%), moderate 30 (52.63%) and severe 22 (38.59%). The *Odds Ratio* (OR) calculated to verify the chance of occurrence of drug interactions in prescriptions with the use of five or more drugs was 8.0, as shown in Chart 1. Thus, the chance of drug interactions occurring was eight times greater in prescriptions with five or more drugs, with p <0.0001.

Distribution by time

Figure 1 - Distribution of doses by time (n=1,366), Rio de Janeiro, Rio de Janeiro, Brazil, 2019
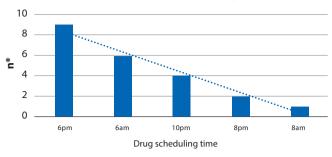
Chart 1 - *Odds Ratio* for the occurrence of potential drug interactions in prescriptions for patients with cardiovascular events, Rio de Janeiro, Rio de Janeiro, Brazil, 2017, n=99

Number of drugs	Prescriptions without PDI	Prescriptions with PDI	*p* value	OR
Up to 5 drugs	33	11	<0,0001	8,0
5 drugs or more	15	40		

Note: PDI - potential drug interactions; OR – Odds Ratio.

Chart 2 - Characteristics of drug interactions with potential for serious harm

Medicament 1	Medicament 2	Documentation	Clinical repercussion	n*
Simvastatin	Amlodipine	Good	Increased risk of myopathy, including rhabdomyolysis;	4
Enoxaparin	Clopidogrel	Fair	Increased risk of bleeding;	4
Amiodarone	Ranitidine	Fair	Increased exposure to amiodarone;	2
Risperidone	Simvastatin	Good	Increased risk of myopathy, including rhabdomyolysis;	2
Diltiazem	Metoprolol	Good	Increased risk of hypotension, bradycardia and changes in atrioventricular conduction;	1
Enalapril	Potassium chloride	Good	May result in hyperkalaemia;	1
Cilostazol	Omeprazole	Good	Increased exposure to cilostazol;	1
Amlodipine	Clopidogrel	Excellent	Decreased antiplatelet effect and increased risk of thrombotic events;	1
Enoxaparin	Warfarin	Fair	It may result in an increased risk of bleeding;	1
Carvedilol	Digoxin	Fair	May result in increased digoxin concentrations; Increased risk of complete heart block;	1
Amlodipine	Amiodarone	Good	May result in bradycardia, atrioventricular block and / or sinus arrest;	1
Simvastatin	Amiodarone	Excellent	Increased risk of myopathy, or rhabdomyolysis;	1
Ticagrelor	Amiodarone	Fair	May result in increased exposure to amiodarone and ticagrelor;	1
Digoxin	Spironolactone	Good	Increased exposure to digoxin.	1
TOTAL:				22

Note: *n - number of times the drug pair was detected by the software.

Severe PDI by drug scheduling times

Note: n* - number of times that drug interaction occurred with severe damage; PDI - potential drug interactions.

Figure 2 - Distribution of severe PDI by drug scheduling times

As for serious interactions, and m 18 drug prescriptions were detected 22 severe PDI, an average of 1.22 serious PDI interactions per prescription. All prescriptions involved (n=18) had five or more prescription drugs. The average number of drugs in the prescriptions where the classification of severe PDI was assigned was 13.33 drugs per prescription. The average drug dose of these prescriptions was approximately 17.72.

Drugs for severe PDI were simvastatin (n=5), amiodarone (n=5), amlodipine (n=4), clopidogrel (n=4), enoxaparin (n=4), digoxin (n=2) , ranitidine (n=2), risperidone (n=2), diltiazem (n=1), carvedilol (n=1), cilostazol (n=1), potassium chloride (n=1), spironolactone (n=1), enalapril (n=1), metoprolol (n=1), omeprazole (n=1), ticagrelor (n=1) and warfarin (n=1).

The drug pairs (n=14) with potential drug interaction for severe damage, plus the level of evidence from the studies that attributed this classification, as well as the possible clinical repercussions that can be observed in the practice of nursing care, can be seen in Chart 2.

It can be seen in Figure 2 that 15 (68%) of potential drug interactions with severe damage were scheduled for 6 p.m. and 6 a.m., times when there was a higher number of doses scheduled by nurses.

DISCUSSION

With regard to socio-demographic and clinical characteristics, the care profile at the locus inpatient unit of the research, marked by a greater predominance of male patients, with a mean age of 71.7 years and the prevalent diagnosis of heart failure points to an audience of elderly patients with chronic non-communicable disease.

Such a profile, in the interface with the investigated phenomenon of drug interactions, signals a risk factor for interactions that is polypharmacy, since the age linked to the prevalence of chronic non-communicable diseases requires the association of several drugs, reflecting on care of nursing with regard to scheduling performed by nurses. In the screen survey, prescriptions with severe PDI had five or more prescription drugs, which characterizes polypharmacy.

This statement is consistent with results of national and international investigations[7,19-20]. This is the case of the research that characterized polypharmacy in primary care users and identified the factors associated with it. There was a prevalence of 9.4% of polypharmacy in the general population and 18.1% in elderly

people over 65 years. The presence of chronic diseases, such as heart disease, was a statistically significant factor associated with polypharmacy[7].

In the second survey, it was found that among 44 elderly people with chronic health conditions who had their prescription evaluated, 50% had polypharmacy and 72.7% at least one potentially inappropriate drug prescribed. Therefore, this profile leads to the need for professional (re)knowing the physiology of aging, the expected morbidities for this age group, the drugs used in this clientele and the most common ones in the field in which they are inserted[19], with a view to preventing errors related to drug interactions.

In this understanding, specifically about heart failure, the disease most found among patients in this study, it is a worldwide phenomenon, with a high rate of occurrence in the population and high rates of hospitalization and mortality. Regarding this condition, the results of the investigation that identified the clinical-epidemiological profile and the treatment instituted between surviving and non-surviving patients hospitalized with heart failure stand out, comparing them to data from the international literature[21].

The treatment followed the current guidelines, which provide for the use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and beta-blockers in systolic heart failure. The use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers at admission was higher among survivors[21].

These findings are in line with that identified in the drug therapy proposal present in the analyzed prescriptions of patients with cardiovascular events in this research, mainly heart failure, as the main drug classes prescribed were antihypertensive drugs, analgesics, diuretics and antiplatelet agents.

The most frequent antihypertensives were: calcium channel blockers (amlodipine and diltiazem), beta-blockers (atenolol, metoprolol and carvedilol), angiotensin-converting enzyme inhibitors (captopril and enalapril), angiotensin receptor antagonists (losartan) and adrenergic blockers (methyldopa). This profile medicated approaches to the last guideline for heart failure of the Brazilian Society of Cardiology[5].

Regarding the schedules carried out by nurses, despite the balance in the distribution of doses in relation to scheduling by shifts (51% of doses scheduled for the day shift and 49% for the night shift), in the analysis of the distribution by time in each work shift, it was noted that the prevalent time in the day service was at 6 p.m. and in the night service at 6 a.m. The least scheduled time in the day service was at 16 hours with 58 doses, and in the night service at 2 hours with 8 doses. Between 14 and 16 hours there was a significant drop-in doses scheduled during the day and in the night service between 24 and 04 hours.

This result is similar to that of other investigations carried out on drug scheduling in hospitalization scenarios. In one of them, performed in intensive care, there was a predominance of scheduling for the night service (57.11%), with a concentration in the hours of 06 hours (29.18%) and 22 hours (17.86%)[15].

Another example was the investigation of scheduling and its association with drug interactions in the context of analgesic therapy with opioids in burn patients, in which 272 medical records were analyzed. The concentration of doses occurred at 22 and 06 hours and this favored the occurrence of PDI (frequency

of 66%, 88.8% being severe) with an increased chance of causing respiratory depression in three times[22].

When carrying out the analytical deepening of the distribution of drug scheduling in this research, it is assumed that the drop in doses in the afternoon is linked to the institution's family visit time and the receipt of drugs from the pharmacy. This is because, the prescription is sent up to 12 hours to the pharmacy and returned with the separate drugs between 2 and 4 p.m., thus coinciding with the family visit time.

The drop-in doses scheduled during this period may be related to these structural conditions, as the nursing team is directed to assist patients and their families, monitor the flow of visits, receive, check and distribute drugs in patients' drawers, request absences and check for possible errors in the delivery of drugs.

As for the night service, it is conjectured that the drop in scheduled doses between 24 and 04 hours has links with nurses' attempt of to reconcile the drug administration times with the home routine, as many patient's inpatient units are in preparation for hospital discharge. Furthermore, the routine of nursing care in the night service is influenced by the characteristics of this shift, particularly the reduction in the nursing team and the rest time, factors that interfere in the choice of drug schedules.

These points lead to the belief that nursing practice is organized based on aspects of the team's dynamics and institutionalized routine. Thus, from the perspective of safety, are latent conditions in this system[17] that influence decision making when scheduling drugs, which makes it necessary to discuss such nursing care in a systemic approach, considering the vulnerabilities environmental/ institutional[17].

In this sense, an aspect that deserves to be discussed is the use of electronic drug prescriptions, considered one of the solutions for improving patient safety in relation to drugs. A study demonstrates that this computerization of prescriptions by means of intelligent software facilitates the work process, the standardization of language, the improvement of the interrelation of professionals, the clarity of information and the security of information recording[23].

In addition, the software may contain automatic features that indicate inadequacies in prescriptions in relation to the scheduled times, toxic doses, treatment time, adverse effects, potential interactions[23]. On the other hand, electronic prescription also has limitations. In the research scenario, for example, in which nurses select the times for scheduling drugs through the computerized system, the times available for selection are pre-determined by such a system, with no possibility of proposing new times, which also affects when scheduling the use of odd hours.

Despite these conditions linked to management, it is recognized the importance of nurses to know the current need of the patient and his clinic, the drug class and the therapeutic purpose of the drugs involved in the prescription, as well as the chance of drug interactions and their possible outcomes.

Moreover, nursing surveillance of the prescribed drugs regardless of the schedule is essential. This is because when considering the therapy and the amount of drugs that need to be prescribed, at some point, these drugs will be found on the schedule. Therefore, it is the role of nurses to monitor reactions and prompt intervention.

This monitoring is one of the pillars of safety in the use of drugs, particularly in the item that deals with the right answer, which recommends: carefully observing the patient to identify, when possible, if the drug had the desired effect; record in medical records and inform the prescriber of all effects different from those expected for the drug; maintain clear communication with the patient and/or caregiver; consider the observation and report of the patient and/or caregiver about the effects of the drugs administered, including responses different from the usual pattern; record all appropriate monitoring parameters[17].

The higher concentration of drug doses between 6 p.m. and 6 a.m. should generate professionals to reflect on the potential implications in relation to patient safety. Therefore, it requires vigilance to detect immediate adverse reactions arising from the administration of the drug, as well as to record it in the medical record, in addition to monitoring the appropriate monitoring parameters.

Regarding the occurrence of PDI's, of the total sample analyzed (n=99), 51 prescriptions presented drug interactions. The chance of drug interaction occurring in prescriptions with five or more drugs was eight times greater than in prescriptions with less than five drugs, which is in line with other studies in this field[9-10].

Severe PDI's accounted for 38.59% (n=22) of the total drug interactions identified in the survey. Studies supporting the discussion corroborate the results of the research on screen, which showed a high rate of serious drug interactions and antihypertensive, antiarrhythmic, antiplatelet agents, statins and anticoagulants the classes that were most involved in the interactions, especially amlodipine + simvastatin and enoxaparin + clopidogrel.

In an international study carried out in a cardiology ward in an Indian teaching hospital, 812 prescriptions from patients who were hospitalized for at least 48 hours were analyzed to assess potential drug-drug interactions. The study identified 388 interactions, of which 7.20% were classified as mild, 60.30% moderate and 32.50% severe. The classes most involved in interactions are antiplatelet agents, anticoagulants and diuretics[20].

This result is similar to that of research on drug interactions in patients hospitalized with heart disease in a Pakistani hospital, in which the most prevalent drug pairs were: aspirin + clopidogrel, clopidogrel + fondaparinux and aspirin + fondaparinux[9]. Nationally, research already carried out with cardiac patients also shows similarities to these results.

An investigation that illustrates this is the prevalence and clinical significance of drug interactions in the prescriptions of 40 elderly hypertensive patients followed up in a basic health unit in São Paulo. 169 interactions were detected and each elderly participant had at least one interaction. As for severity, 29 interactions were classified as serious, equivalent to 17.2%. The most frequent serious interaction was that of amlodipine with simvastatin (15%) and the drugs most involved in the interactions: acetylsalicylic acid, enalapril, hydrochlorothiazide, glibenclamide, metformin, simvastatin, amlodipine, captopril and furosemide[8].

Some of these classes of drugs were also present in the research carried out with patients with coronary artery disease who were followed up on an outpatient basis at *Instituto do Coração* (Heart Institute), to analyze the prevalence, severity and the implications of drug interactions. The researchers found that the main

interactions occurred with beta-blockers (43.3%) and angiotensin-converting enzyme inhibitors (27.8%), angiotensin-converting enzyme inhibitors + acetylsalicylic acid (63.3%), and beta-blockers + blockers calcium channels (28.9%), most of them of moderate severity, with a recommendation for to monitor therapy[6].

The clinical repercussions of the identified interactions include: bleeding, changes in heart rhythm, vital signs, thrombotic events, myopathy, rhabdomyolysis, digoxin toxicity. Such repercussions in elderly patients with cardiovascular events, who already have the body systems affected by their condition, may further limit their clinical evolution.

These damaging effects of interactions have not been well studied. This is what a systematic review states about the prevalence of potential drug interactions and those that resulted in damage to the patient during hospitalization, carried out based on 27 articles published between 2000 and 2016. It was not possible to determine the prevalence of interactions that caused real damage to the patient, as the existing data was limited. The authors indicated the need for studies that could go beyond measuring interactions, but assess their impact on patients[24].

One of the studies that measured this impact was the one that analyzed the presence of drug interactions in patients in the cardiology ward and followed them up to identify the evidence of the interactions. The prevalence of interaction was 30.47% involving 249 patients, and the most common were heparin + aspirin (29.38%) and clopidogrel + heparin (7.21%). Therefore, 68 real cases were detected, with an incidence of 17.53%, with bleeding being the most common adverse effect with 60 cases, mainly due to heparin and warfarin[20].

Therefore, considering that the peak time of occurrence of interactions was at 6:00 p.m. and at 6 a.m., scheduling times most used by nurses for drug administration, and that the average number of drugs in prescriptions in which severe drug interaction occurred was 13.33, nurses when scheduling drugs needs to carefully evaluate the elements contained in the drug prescription. In this understanding, knowledge about drug interactions is paramount.

Study limitations

It is methodological, in relation to the number of prescriptions, since in the research on screen, it was decided to analyze a single prescription with 48 hours of hospitalization. Therefore, this choice restricted the number of prescriptions, the identification of other potential findings related to the interactions and their links with the schedule carried out by nurses.

Contributions to nursing

The drug interactions detected refer to the need to think about the factors that may have affected its occurrence, such as issues related to specific knowledge acquired since academic training, the use of schedules based on institutional routines, aspects of the work process, the physical structure of the place where the appointment is made, the difficulty of communication between doctors, nurses and pharmacists.

Therefore, to minimize the occurrence of interactions, these factors must be evaluated through a systemic approach, so that, from that point on, interventions in reality can be proposed in view of patient safety. In the case of the investigated reality, these interventions go beyond the need to adapt the electronic drug system implemented in the institution, with the insertion of automatic alerts that signal frequent drug interactions to the team in the daily practice of patients with cardiovascular events, in light of the profile identified; the discussion of drug scheduling and the occurrence of drug interactions in the context of teaching through the simulation of clinical cases, with analysis of common situations in daily nursing, to develop the ability to make decisions regarding care based on clinical reasoning, combining theory and practice; joint performance of professionals, with the participation of the clinical pharmacist.

CONCLUSIONS

There is still a practice in which there is no diversification of schedules for the administration of drugs, which makes patients hospitalized for cardiovascular causes vulnerable to drug interactions, particularly serious ones. This was evidenced by the occurrence of serious interactions in 22 drug pairs, mainly in prescriptions that had five or more drugs and more frequently at 6 p.m. and 6 a.m., times with higher dose scheduling performed by nurses. The most recurrent drug pairs involved in serious interactions were simvastatin + amlodipine and enoxaparin + clopidogrel.

These results point out that the practice of nursing with regard to scheduling drugs requires a review of the criteria for proposing schedules, considering a wide range of possibilities, in view of ensuring patient safety.

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