Potential drug-food interactions in patients hospitalized in the Cardiology Unit

Potenciais interações fármaco-alimento em pacientes internados no Setor de Cardiologia

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A B S T R A C T

Objective

To analyze potential Drug-Food Interactions identified in prescriptions of patients admitted to the Cardiology Unit of a university hospital.

Methods

This is a descriptive, cross-sectional quantitative study carried out in the Cardiology Unit of a university hospital in the city of *Rio de Janeiro*, Brazil. Data collection took place in archived medical records of hospitalized patients between August and September, 2016.

Results

In each prescription, there were on average 7.5 drugs mentioned (Standard Deviation of 2.1). Most were tablets (93%) and antihypertensive drugs (40%). Two hundred and fifty two potential Drug-Food Interactions were identified. Acetylsalicylic acid and omeprazole were the most potentially interactive drugs.

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Conclusion

Drug-Food Interactions occur with commonly used drugs, for example omeprazole and acetylsalicylic acid. However, health teams do not know or identify a substantial part of interactions. This factor leads to an exposure to risks related to changes in drug response and patient safety.

Keywords: Administration, oral. Cardiology service, hospital. Food-drug interactions. Nursing. Patient safety.

R E S U M O

Objetivo

Analisar as potenciais interações fármaco-alimento identificadas a partir das prescrições medicamentosas de pacientes internados no Serviço de Cardiologia de um Hospital Universitário.

Métodos

Trata-se de um estudo quantitativo, descritivo e transversal, realizado em uma unidade de internação cardiológica de um Hospital Universitário localizado no município do Rio de Janeiro. A coleta de dados ocorreu em prontuários arquivados de pacientes internados entre agosto e setembro de 2016.

Resultados

Em cada prescrição haviam em média 7,5 medicamentos, desvio padrão de 2,1, sendo a maioria comprimidos (93%) e da classe dos anti-hipertensivos (40%). Identificou-se 252 potenciais interações fármaco-alimento, sendo o ácido acetilsalicílico e omeprazol os medicamentos de maior potencialidade de interação.

Conclusão

As interações fármaco-alimento ocorrem com medicamentos comumente utilizados, a exemplo do omeprazol e ácido acetilsalicílico. No entanto, parte substancial das interações não são conhecidas ou identificadas pela equipe de saúde, colaborando para exposições aos riscos de alterações na resposta medicamentosa e na segurança do paciente.

Palavras-chave: *Administração oral. Serviço hospitalar de cardiologia. Interações alimento-droga. Enfermagem. Segurança do paciente.*

I N T R O D U C T I O N

Food nutrients exert important actions in the human organism, for they participate in the structural and functional restoration of organic activities. However, the concomitant ingestion of food with medicinal products may alter their functions, as well as the pharmacokinetics and pharmacodynamics of drug compounds. Such convergence in the living organism is known as Drug-Food Interaction (DFI) [1].

Drug-Food Interactions are facilitated because most drugs are prescribed orally, and are generally administered concomitantly with food. This concomitance may directly affect nutrition and drug actions, generating risks such as pharmacological toxicity, severe malnutrition, increase in the costs of treatment, a longer hospital stay, among others [2].

Considering the potentiality of risks, the American Hospital Accreditation Organization, The Joint Commission, has encouraged health professionals to monitor possible DFIs in hospitalized patients since the 1980s [3].

The importance of such monitoring is exemplified especially with elderly patients admitted to the cardiology unit. Diseases such as heart failure may lead to a concomitant use of five or more drugs (polypharmacy), which directly increases the potential for the occurrence of DFIs [4,5].

Controlling and mitigating DFIs are important challenges for the health care team in the hospital environment. Nonetheless, nursing protagonism is relevant for being ahead of the supply and evaluation of food acceptability, besides having the challenge of being the professionals who are responsible for drug administration, and must therefore guarantee to the hospitalized patient a continuous and harmless care [2,3].

In this perspective, the occurrence of a DFI immediately results in pharmacovigilance and nutritional vigilance. The multiprofessional team should pay close attention not only to possible drug-drug interactions, but also to DFIs [2,3].

Thus, the objective of this study is to analyze potential drug-food interactions identified in prescriptions of patients admitted to the cardiology unit of a university hospital.

METHODS

This is a quantitative, cross-sectional, exploratory study on a Cardiology Unit comprising 28 beds of a university hospital in the city of *Rio de Janeiro*, Brazil.

Working with inpatients was a choice based on the organizational rigor in controlling the dietary and drug administration schedules, which validates the mapping of potential DFIs.

Data collection was performed in October 2016 through the mapping of inpatient prescriptions. For that, a consultation was carried out in medical records of patients hospitalized from August to September 2016.

During this period, 76 patients were hospitalized. In order to determine the number of medical records required to compose a sample, a sample calculation was made using a 5% error and a 95% confidence level. A sample of 64 medical records was thus determined. The inclusion criteria were established as: pres. Illegible prescriptions have been deleted.

The choice of 64 medical records was randomly performed, and the first prescription of the first day of the patient's hospitalization was chosen from each record. Through selection, there were no sample losses. All prescriptions were in compliance to the established criteria for the study.

It is highlighted that the choice of the prescription of the first day of hospitalization was due to the fact that hospital staff generally records a larger quantity of prescribed drugs compared to other days [5], which contributes to a better stratification of potential DFIs.

With the support of a standardized form, information regarding the characterization of patients such as gender, age, comorbidities, reasons and length of hospitalization was extracted from the medical record. In the prescriptions, oral drugs were discriminated, with information on description, dosage, and schedule of administration.

To establish interactions between drugs and foods, scientific articles on the subject were used as a basis, as well as the Micromedex Drug Interactions® software. By means of data collection, a descriptive statistical analysis of the results was carried out.

This study is part of an integrated research project entitled Good practices applied to patient safety: a drug administration study. The Research Ethics Committee of the institution, registration No.336.436 - *Certificado de Apresentação para Apreciação Ética* (CAAE) No.17589513.0.0000.5238, approved the study.

R E S U L T S

The results are presented in three segments: characterization of hospitalized patients, profile of drug prescriptions, and mapping of drug-food DFIs.

Characterization of hospitalized patients

The study consisted of 36 men and 28 women, with individuals between 61 and 80 years-old as the highest recurrence (50.0%). Of the total number of applicants, 43 individuals had hypertension, 25 had diabetes, and 24 had cardiopathy as underlying diseases. At hospital admission, the most relevant justifications were heart failure (17.1%) and dyspnea caused by effort (12.5%), with an average length of stay of 11 to 20 days (48.4%).

Profile of drug prescriptions

As for drugs, 483 were prescribed orally. The majority of them(93%) were tablets. Among other pharmacological presentations, there were capsules, coated tablets, and drops (Table 1).

On average, each prescription contained 7.5 oral drugs (a minimum of three drugs and a maximum of 13 drugs), with a Standard Deviation (SD) of 2.1 and a variance of 4.5. Of these drugs, 40% were antihypertensives, followed by antiulcers (8%), the former being the class of highest recurrence (Figure 1).

In all 64 prescriptions, 606 administrations were performed on different schedules. From 06:00 to 11:00, 253 (41%) drugs were administered; from 12:00 to 17:00, 127 (21%) drugs; and from 18:00 to 23:00, 199 (32%) drugs. The distribution of schedules can be observed in Table 2.

Mapping of Drug-Food Interactions

Of the drug classes with the greatest recurrence in prescriptions (analgesics, antipyretic, antiplatelet, antihypertensive, antiarrhythmic, anticoagulant, antitilipemic, antithrombotic, antiulcer, and coronary vasodilators), there were 252 potential interactions between drugs and food/nutrients.

Table 1. Pharmacological presentation of prescribed drugs. *Rio de Janeiro* (RJ), Brazil, 2016.

Pharmacology	Af	Rf
Capsules	11	2.3
Tablets*	452	93.6
Coated tablets	10	2.1
Drops	6	1.2
Solutions	1	0.2
Syrups	3	0.6
Total	483	100.0

Note: *Higher Tablet frequency.
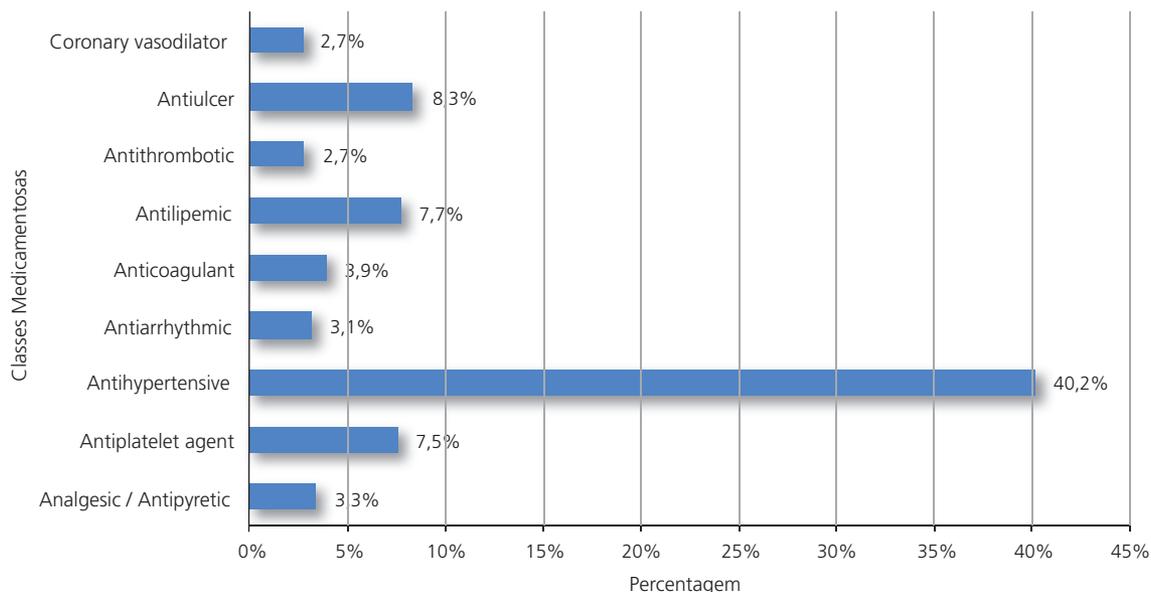Af: Absolute Frequency; Rf: Relative frequency - %.

Figure 1. Distribution of drug classes with the greatest rates in prescriptions. *Rio de Janeiro* (RJ), Brazil, 2016.

Table 2. Administration of drugs and respective schedules according to drug prescriptions. *Rio de Janeiro* (RJ), Brazil, 2016.

Times of administration	Af	Rf
00:00 to 05:00	27	4.5
06:00 to 11:00*	253	41.7
12:00 to 17:00	127	21.0
18:00 to 23:00*	199	32.8
Total	606	100.0

Note: *Higher frequency administration of drugs.

Af: Absolute Frequency; Rf: Relative frequency - %.

The drugs with the greatest potential for drug-food interaction were acetylsalicylic acid (13%) and omeprazole (13%). Also noteworthy were atenolol (9%), carvedilol (8%), spironolactone (8%), hydrochlorothiazide (7%), and warfarin (7%) (Table 3).

Table 3. Distribution of potential DFI and mechanism/effect of interaction. *Rio de Janeiro* (RJ), Brazil, 2016.

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Drug	Food/Nutrient	Mechanism/Effect	Potential interaction	
			Af	Rf
Analgesic/Antipyretic				
Dipyrone	Does not interact with food	_____*	0	0.0
Antiplatelet agent				
Acetylsalicylic Acid (ASA)	Vitamin C and Vitamin K	Depletes vitamin absorption	34	13.5
Cilostazol	Rich in fats	Increases drug absorption	2	0.7

Table 3. Distribution of potential DFI and mechanism/effect of interaction. *Rio de Janeiro* (RJ), Brazil, 2016.

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Drug	Food/Nutrient	Mechanism/Effect	Potential interaction	
			Af	Rf
Antihypertensive				
Anlodipine	Calcium, Potassium and Vitamin D	Depletes vitamin and mineral absorption	16	6.4
Atenolol	Food in general	May interfere with the plasma concentration of the drug	24	9.5
Atensine	Does not interact with food	_____*	0	0.0
Bisoprolol	Does not interact with food	_____*	0	0.0
Carvedilol	Food in general	Decreases gastrointestinal discomfort and orthostatic hypotension	22	8.7
Captopril	Food in general	Decreases drug absorption	12	4.8
Clonidine	Does not interact with food	_____*	0	0.0
Diltiazem	Food in general	Promotes drug absorption	3	1.2
Doxazosin (Carduran)	Does not interact with food	_____	0	0.0
Enalapril	Does not interact significantly with food	_____	0	0.0
Spironolactone	Food in general	Promotes drug absorption and retains potassium	21	8.3
Furosemide	Food in general	Decreases drug absorption	16	6.4
Hydralazine	Does not interact significantly with food	_____*	0	0.0
Hydrochlorothiazide	Food in general	Increases drug absorption	19	7.5
Losartan	Does not interact significantly with food	_____*	0	0.0
Metoprolol	Does not interact significantly with food	_____*	___*	__*
Nifedipine	Food in general (mainly grapefruit)	Increases the drug action time	1	0.4
Valsartana (Brasart)	Does not interact significantly with food	_____*	0	0.0
Antiarrhythmic				
Amiodarone	Food in general (mainly grapefruit)	Increases drug bioavailability	9	3.6
Digoxin	High-fiber foods	Decreases absorption and peak serum concentration	6	2.4
Anticoagulant				
Warfarin	Vitamin K-rich foods	Decreases anticoagulation	18	7.1
Antilipemic				
Simvastatin	Grapefruit	Decreases drug bioavailability		
Atorvastatin	Does not interact significantly with food	_____*	0	0.0
Antithrombotic				
Clopidogrel	Does not interact with food	_____*	0	0.0
Antiulcer				
Omeprazole	Vitamin B_{12} and iron	Decreases absorption of Iron and Vitamin B_{12}	33	13.1
Ranitidine	Vitamin B_{12} and iron	Decreases absorption of Iron and Vitamin B_{12}	7	2.8
Coronary vasodilator				
Isosorbide monitrate	Food in general	Decreases drug absorption	9	3.6
Propatilnitrate (Substrate)	There are no studies demonstrating interactions with food	_____*	___*	
Total of possible interactions			252	100.0

Note: ___*No known interaction with food, no mechanism of action or effect in the human organism.

Af: Absolute frequency; Rf: Relative frequency - %.

DISCUSSION

Currently, the Brazilian population undergoes changes in its demographic profile because life expectancy has increased year after year. It is estimated that the average life expectancy of Brazilians will be 80 years until 2025. With such an increase, there is also a change in the epidemiological profile. Chronic-degenerative diseases have become one of the main causes of morbidity and mortality, especially among the male population, which is the most vulnerable population group to such diseases [6,7].

The characterization of the studied population corroborates the current demographic and epidemiological profile of Brazil. Fifty percent of the studied individuals were between 61 and 80 years-old. Most were men (56%) with chronic diseases such as arterial hypertension, diabetes *mellitus*, and cardiopathies.

Regarding the reasons for hospital admission, heart failure (17%) and dyspnea caused by effort (12%) were the main causes, which is in line with studies that have evidenced that cardiovascular diseases are the main reasons for admissions in the *Sistema Único de Saúde* (SUS, Brazilian Unified Health System). Heart failure is the most prevalent cardio-circulatory disease in Brazil [4].

Hospital admission is a measure to recover health. At the same time, the longer the hospitalization time, the greater the risks of complications and injuries to the patient. In addition, the quality of care is related to time, with a mean acceptable period of 6.6 days [8] being stipulated nationally. In the present study, the patients' stay was above average: 48% had been hospitalized for 11 to 20 days.

Patients in hospital admission receive, during the whole period, adequate drugs and food for the reestablishment of their clinical condition. However, some factors may trigger the ineffectiveness of nutritional and/or pharmacological treatment, such as the occurrence of DFIs. The risks of such interactions are greater among the elderly with chronic diseases requiring polypharmacy [2,9].

The most frequently occurring DFIs in the hospital environment are related to changes in the absorption rate of drugs, especially in protein-, fat- and fiber-rich diets, by altering the gastric pH and the gastrointestinal motility, as well as changing important transport proteins [10].

In contrast, some DFIs benefit treatment, since some foods can reduce irritation of the gastrointestinal mucosa, favoring drug absorption [11].

Drugs administered orally are absorbed mainly through the gastric mucosa and the small intestine. These are the priority sites for the occurrence of DFIs, since food and drugs undergo similar absorption processes in the body [2,11].

This is because most drugs are prescribed orally, especially as solids, due to ease of use, low cost and greater adherence to treatment [12]. This is confirmed by the results of this study: 93% of the drugs were tablets, followed by capsules (2%) and coated tablets (2%).

Another factor that may influence drug and/or dietary absorption is the amount of drugs prescribed. When the prescription exceeds three different drugs, there is a greater possibility for the occurrence of DFIs. It may change the drug's effectiveness and generate nutritional deficiency [13]. Regarding the data, each prescription contained on average number of 7.5 drugs, which exponentially increased the chances of a potential drug-food interaction.

The large number of drugs in prescriptions is related to the characteristic of polypharmacy of cardiology patients [14]. Research shows that most patients admitted to the cardiology unit take

antihypertensives, being this group the one with the greatest recurrence of prescriptions in the present study [14,15].

Drug prescription is organized at different times according to the schedule made by nurses. Most drugs are scheduled for between 06:00 and 22:00, with a higher concentration in the early morning and late evening [16].

Such predominance appears in the results of this study: most drug administrations occurred from 06:00 to 11:00, and from 18:00 to 22:00. The concentration of drugs during these windows increases the occurrence of DFIs because, in this period, the main hospital meals are provided, which increases the risk of concurrent eating and drug use [13].

DFIs are difficult to identify and recognize, which increases the risk of impairment to the drug and/or food action [11,12]. Thus, it is necessary to know and identify potential DFIs so that the success of the nutritional and pharmacological therapy can be facilitated.

Two hundred and fifty two potential interactions were identified. The most recurrent drug classes in the studied unit are antihypertensives (40%), antiulcer (8%), antilipemic (7%), and antiplatelet agents (7%). Of these, the drugs that were most likely to interact were acetylsalicylic acid (13%) and omeprazole (13%). Atenolol (9%), carvedilol (8%), spironolactone (8%), hydrochlorothiazide (7%), and warfarin (7%) also stood out.

Among the drugs with the highest recurrence and interaction probability is Acetylsalicylic Acid (ASA). It is an antiplatelet agent that interacts specifically with vitamin C (found in citrus fruits and some vegetables) by reducing absorption and increasing the excretion of this vitamin. There is also an interaction with vitamin K (present in vegetables and oils), reducing the organic reserves of this nutrient and causing an increase in the excretion of thiamine, folic acid, and amino acids. It is recommended not to eat foods rich in vitamin C and K concomitantly or close to the use of ASA, giving preference to using ASA in mealtime intervals [2,13].

Omeprazole, which belongs to the antiulcer class, interacts with vitamin B12 (found at higher amounts in animal proteins) and iron (present in animal, legume, and vegetable proteins), causing depletion and consequently a low absorption of these nutrients. Therefore, in order to avoid such interaction, it is necessary not to use omeprazole together with foods that are sources of vitamin B12 and iron. There should be a period of one or two hours after their ingestion [2,11,17].

Among antihypertensive drugs, four drugs stood out: atenolol, carvedilol, spironolactone, and hydrochlorothiazide. Atenolol interacts with food in general, as it may change the plasma concentration of the drug, decreasing its absorption. It needs to be administered hours after meals [2,11,18].

Spironolactone interacts with food in general, favoring the absorption of the drug, but with retention of potassium. Therefore, it is recommended not to administer the drug together with foods which are rich in this nutrient, such as avocado and banana [2,11,18].

Carvedilol and hydrochlorothiazide, on the other hand, have a beneficial DFI. Their concomitant use is recommended since the contact between food in general and carvedilol reduces gastrointestinal discomfort and orthostatic hypotension caused by the drug, and when in contact with hydrochlorothiazide, it favors its absorption [2,11,13,18].

Finally, warfarin, which belongs to the class of anticoagulants, is the most described and known drug when it comes to DFIs. Achieving optimal therapeutic levels of this drug is difficult as it may interact with a wide variety of foods. The best known interaction is with vitamin K (present in vegetables such as broccoli, cabbage, parsley, and spinach). It reduces the effect of the drug, promoting blood clotting and increasing risks of thrombus [14,19].

CONCLUSION

Scientific knowledge about drug-food interactions is extremely important since drug-food interactions occur with commonly used drugs and foods, such as the interaction between omeprazole and vitamin B_{12}, found in most animal proteins, and of acetylsalicylic acid with vitamin C and K, which are present in citrus fruits and some vegetables and oils, respectively.

It should be noted that some interactions might bring benefits, such as interactions with carvedilol and hydrochlorothiazide. When used concomitantly with food, they reduce gastric discomfort as food favors drug absorption.

Therefore, through the description and identification of potential drug-food interactions in the cardiology unit, this study was able to evidence the need for a better training of the multiprofessional team. Based on a better knowledge on the subject, a safer and harmless care can be provided.

CONTRIBUTORS

MK ANJOS was responsible for the design and conception of the research project, for the collection, analysis and interpretation of data, and for writing this paper. TCSS OLIVEIRA and MB MOREIRA were responsible for data collection. SO MOREIRA was responsible for reviewing this study. MAC STIPP was responsible for writing and critical review. GO PAES was responsible for research guidance, writing and critical review.

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ERRATUM

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