Original Paper

Evaluation of potential drug interactions in hospital admission

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Abstract

Introduction: In clinical practice, drugs association is common and can lead to drug interactions (MI), which can lead to an avoidable adverse events that may need a for pharmaceutical intervention. **Objective:** The objective of this study is to identify and evaluate the drug interactions present on prescriptions of patients at the adult medical clinic of a hospital in Rio de Janeiro, at admission moment. **Method:** Cross-sectional study involving the analysis of information through the database (e-sus). Interactions were classified according to the Micromedex database. **Results:** A total of 177 prescriptions were evaluated. The main underlying disease was the neoplasias (36.16%), and the main cause of hospitalization was pain (8.5%). Of the prescriptions evaluated, 81.93% had some potential MI. A total of 180 types of MI were identified, representing 600 IM. Considering the degree of severity, 60% (358) were classified as severe MI, 38% (229) moderate, 1% (7) low and contraindicated. The most prevalent drug involved in MI was dipyrone (43.8%). The most frequent severe MI was between Dipirona + Enoxaparin (9.4%). Among moderate MI, Dipirone + Captopril (14.8%) was the most frequent and among the low ones, Furosemide + Hydralazine (42.9%). The contraindicated MI appeared in a similar way with 16.7% each. According to the scientific evidence found, serious MI had mostly reasonable documentation (59.5%), while the moderate ones had the majority of documentation classified as good (48.9%). **Conclusion:** In this context it is reasonable to consider that the pharmaceutical analysis of prescription at the patient admission may contribute to preventing drug-related adverse events.

Keywords: Drug Interactions, Medications errors, Drug Utilization.

Avaliação de potenciais interações medicamentosas na admissão hospitalar

Resumo

Introdução: Na prática clínica, a associação de medicamentos é comum e pode acarretar em interações medicamentosas (IM), que podem ocasionar eventos adversos evitáveis passíveis de intervenção farmacêutica. **Objetivo:** O objetivo deste trabalho foi identificar e avaliar as interações medicamentosas, na admissão hospitalar, de pacientes da clínica médica de adultos de um hospital do Rio de Janeiro. **Método:** Estudo transversal, envolvendo a análise de informações através do banco de dados (e-sus), As interações foram classificadas segundo a base de dados Micromedex. **Resultados:** No total foram avaliadas 177 prescrições. A principal doença de base observada foi a neoplasia (36,16%), e a ocorrência dor (8,5%) foi o principal motivo de internação. Das prescrições avaliadas 81,93% tinham alguma IM potencial. Foram identificados 180 tipos de IM. No total foram quantificadas 600 IM. Considerando o grau de gravidade, foram observadas neste estudo 60% (358) de IM graves, 38% (229) moderadas, 1% (7) leves e contraindicadas. O fármaco de maior prevalência nas IM foi a dipirona (43,8%). A IM grave mais frequente foi entre Dipirona associada a Enoxaparina (9,4%). Entre as IM moderadas a mais frequente foi a Dipirona associada a Captopril (14,8%) e entre as leves foi Furosemida associada a Hidralazina (42,9%). As contraindicadas apareceram de forma semelhante com 16,7% cada uma. De acordo com as evidências científicas encontradas IM graves apresentaram majoritariamente documentação razoável (59,5%), enquanto as moderadas tiveram a maior parte de documentação classificada como boa (48,9%). **Conclusão:** Neste contexto é razoável considerar que, a análise farmacêutica da prescrição no momento da admissão do paciente possa contribuir na prevenção de eventos adversos relacionados a medicamentos.

Palavras-Chave: Interações de medicamentos, Erros de medicação, Uso de medicamentos

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Introduction

Increasing population longevity has led to the onset of diseases that mainly affect the elderly population.[1,2] There was also an increase in drug demand, stimulated by irrational and unnecessary use, and self-medication.[3] These practices can have a negative impact on population health, including adverse events.[3]

In the clinical practice, drug combination is common and can lead to drug interactions (DIs), which are clinical events that occur when one or more drugs interact with each other or with food, drink, or the environmental factor.[4,5,6] Such changes interfere with drug efficacy or toxicity and may have serious consequences for the patient.[6]

DIs can be beneficial, contributing to the success of treatment, or undesirable, presenting the failure or progression of the disease, which can cause harm to the patient's health, as well as increase the cost of therapy.[6] When detected, DIs may be subjected to pharmaceutical intervention to optimize drug therapy.[7]

There are many variables for the onset of a DI, such as pharmacological agents, multiple prescriptions, use of non-prescription drugs, non-adherence to treatment, drug abuse, and self-medication.[8,9]

A US study has shown that among the top ten causes of death are those caused by adverse drug events, costing the hospitals approximately 5.6 million a year.[10] In recent years, there has been increasing concern about the risks of DIs in the hospital environment. Thus, the development and implementation was initiated of computerized programs and of the presence of the clinical pharmacist for the pharmacotherapeutic follow-up of patients.[8]

During hospitalization other medications that were not part of the previous therapy may be prescribed.[11] Changing care levels — the patient leaving the outpatient setting to the hospital or vice versa — is considered a critical process due to failures in continuity of care and information flow.[12] Therefore, care transition activities are important strategies aimed at ensuring the integrality of the services focused on patient safety. [13]

Medication conciliation, at the time of patient admission, is a tool to help reduce adverse drug reaction (ADR) occurrences, reduce discrepancies between pre-use and prescription drugs as well as identify possible DIs.[14]

This study aimed to identify, evaluate and classify drug interactions at hospital admission according to severity and to the degree of scientific evidence, in patients of the adult medical clinic.

Methodology

This is a descriptive and cross-sectional study on drug interactions found at admission in a tertiary general hospital in the city of Rio de Janeiro. The unit has a structure with 10 floors, 243 beds installed, with 204 operational. Data collection took place between September and November 2017.

The study was conducted in the medical clinic sector, which receives outpatients. According to the institutional survey, the average outpatient admission to the adult medical clinic is 55 patients per month. Considering a sample error of 5% and a confidence interval of 95%, the calculated sample size was 109 patients.

The inclusion criteria for the study population were patients older than 18 years old, of both genders, coming from external admission. The following were excluded from the study: pediatric patients, with divergence in the indicated period of hospitalization, readmission or with an unrecovered or poorly readable medical record. The use of herbal medicines was not considered for analysis.

Data collection was performed by collecting information on the hospitalization of patients in adult medical clinics, through the computerized database in the institution (e-sus), considering the following workflow: after the patient's hospitalization, they were referred to the medical appointment in which the medical prescription was generated. After identifying the admitted patients, the prescriptions were forwarded for analysis at the pharmacy.

Patient identification data and prescription drugs were analyzed. The variables collected were date of admission, gender, age, medical records, sector of hospitalization, reason for hospitalization, previous diseases and number and type of DIs.

For the analysis of the DIs the Micromedex® 2.0 application was used, a database which provides information about potential DIs, as well as the mechanism of adverse reactions, their clinical consequences, severity and scientific evidence (excellent, good, reasonable and bad).[15,16]

From the Micromedex® 2.0 classification, DIs are classified as severe (life threatening and needing immediate intervention), moderate (clinical worsening), mild or no risk (when there is no risk to the patient) and contraindicated.[16]

The medications present in the DIs were classified by drug according to the ***Anatomical Therapeutic Chemical*** (ATC) classification system, which consists of dividing drugs into five levels of classification according to the organ or system in which they operate, as well as their chemical, pharmacological and therapeutic properties.[17] In this work, all levels of classification were adopted.

The documented DIs were rated as excellent, good and reasonable and unknown according to Micromedex®.[16] Data were stored and analyzed in Microsoft Excel®. Descriptive statistics tools were employed in the analysis of the results.

This study was approved by the Research Ethics Committee of the Antônio Pedro University Hospital (***Hospital Universitário Antônio Pedro***, HUAP/UFF) according to opinion No. 2153496 in CAAE 67114817.9.0000.5243 in July 2017. Since it was a research with secondary data (medical records), it was not necessary to use the Free Informed Consent Form (FICF).

Results

Prescriptions were collected at the discharge of 186 patients, from September to November 2017. Nine prescriptions were excluded due to divergences in the hospitalization period (7), duplicity (1) and incorrect medical records (1). In total, 177 prescriptions were evaluated, among which there were 28 omissions of information (18 of evolution and 10 of electronic medical records) that were disregarded, because these two variants did not alter data collection and analysis.

Of the 177 patients involved in the study, the majority (58.8%) were male. The mean age was 59.98 years old (Table 1).

Table 1. Characteristics of the patients. Rio de Janeiro, 2017, (N=177).

Information	Descriptive statistics
Age (years old) mean (SD)	59.98 (XXXXX)
Gender n (%)	
Female	73 (41.2)
Male	104 (58.8)
Previous disease n (%)	
Yes	171 (96.6)
No	6 (3.4)

Of the patients studied, 96.6% had some disease prior to hospitalization. Only 6 (3.38%) patients had no previous disease diagnosed at the time of admission. Among the most common underlying diseases in the study population we found neoplasms (36.16%), arterial hypertension (30.51%), diabetes mellitus (DM) (22.10%), peripheral obstructive arterial disease (POAD) and chronic obstructive pulmonary disease (COPD) (5.84%).

The main reasons for hospitalization were the following: pain (8.5%), neurological disorder (6.2%), anemia and dyspnea (5.0%), encephalopathy (3.95%), POAD, fever, urinary tract infection (UTI) and other procedures (3.4%), amputation, diarrhea, infected lesion and sepsis (2.8%), decompensated DM and weight loss (2.6%), decompensation, dehydration, arteriovenous fistula (AVF) failure, hypertension, hematuria, pneumonia, cough, deep vein thrombosis (DVT) and vomiting (1.7%), anasarca, abscess, tiredness, cirrhosis, convulsion, decompensated COPD, cancer staging, hypoxemia, decompensated heart failure, lymph node enlargement, nausea, impaired renal function and tachycardia (1.13%), and other reasons (0.56%).

Of the prescriptions evaluated, 81.93% had some potential DI. These were identified through the Micromedex® application. We identified 180 pairs of different DIs with associated medications, totaling 600 DIs. Regarding severity, 60% (358) were considered severe, 38% (229) moderate, and 1% (7) mild and contraindicated.

Ten drugs that were more prevalent in the DIs: dipyrone (43.8%), bromopride (18.3%), captopril (12.7%), tramadol (11.7%), ondansetron (8%), enoxaparin (7.17%), losartan (7%), ASA, regular insulin (6.8% each) and morphine (6.5%) (Table 2). These results are justified by the care profile of patients with cancer, as previously mentioned.

Table 2. ATC classification of the 10 drugs in most interactions. Rio de Janeiro, 2017, N=600 interactions

Medication	ATC	Total	
		n	(%)
Dipyrone	N02BB02	209	43.8
Bromopride	A03FA04	110	18.3
Captopril	C09AA01	73	12.7
Tramadol	N02AX02	67	11.7
Ondansetron	A04AA01	48	8.0
Enoxaparin	B01AB05	43	7.17
Losartan	C09CA01	42	7.0
AAS	B01AC06	41	6.8
Regular Insulin	A10AB01	41	6.8
Morphine	N02AA01	39	6.5

Figure 1. Most frequent serious drug interactions.

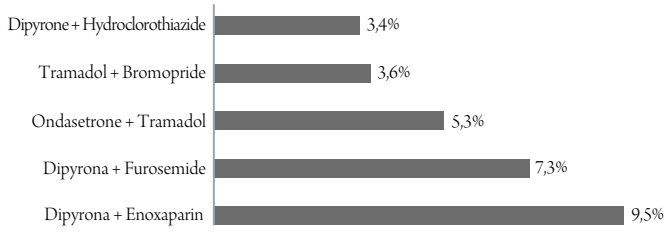
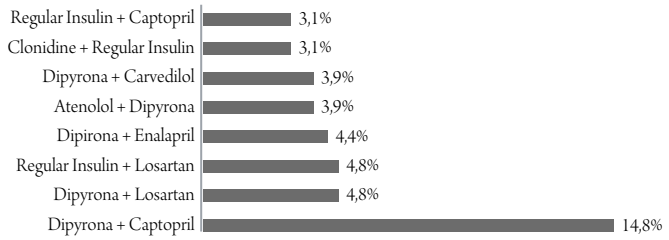


Figure 2. Most frequent moderate drug interactions



The analyses identified seven mild DIs: Furosemide + Hydralazine (42.9%), Dexamethasone + Albendazole, Diazepam + Omeprazole, Atenolol + Calcium Carbonate and Abacavir/lamivudine/Zidovudine +Trimethoprim/Sulfamethoxazole (14.3% each). A similar result was identified by Okuno and colleagues,[19] who identified 12% of mild DIs. It is noteworthy that, usually, these interactions are poorly described in the literature, a fact that may be related to the small impact they represent on the patient's health, requiring only, in most cases, their monitoring.

Six contraindicated DIs were observed: Darunavir + Simvastatin, Ondansetron + Fluconazole, Bromopride + Chlorpromazine, Metoclopramide + Chlorpromazine, Bromopride + Amitriptyline, Bromopride + Fluoxetine (16.7% each).

The adverse reaction highlighted in this type of DI was the extra-pyramidal reaction, and bromopride was involved in half of the contraindicated interactions. This is due to the extra-pyramidal effects associated with this drug.[16]

The DI documentation has been rated as excellent, good and reasonable and unknown according to Micromedex®.[16] There was no presence of unknown documentation.

Evidence was considered reasonable in 47.2% of the DIs, good in 40.2% and excellent in 12.7% of the DIs. Severe DIs presented mostly reasonable documentation (59.5%), followed by good and excellent (34.1% and 6.4%, respectively). Moderate DIs had most of their documentation classified as good (48.9%) reasonable (27.9%) and excellent (23.1%). Mild DIs had their documentation considered as good and those contraindicated as reasonable (Table 3).

Table 3. Documentation classification according to the types of interactions. Rio de Janeiro, 2017, N=600

	Documentation (%)		
Interaction Type	Excellent	Good	Reasonable
Severe	23 (6.4%)	122 (34.1%)	213 (59.5%)
Moderate	53 (23.1%)	112 (48.9%)	64 (27.9%)
Mild	0	7	0
Contraindicated	0	0	6

Discussion

The mean age observed is similar to that observed by Vonbach et al.[12], males prevailing with 53%. In similar studies, Passos et. al.[18] and Okuno et. al.[19] found mostly female patients (61% and 53.5%, respectively).

The profile of drug interactions is similar to that observed in a hospital in Switzerland by Vonbach et al.[12] where 62% of the observed interactions were severe and moderate upon admission. A North American study found 43.6% of severe and 33% of moderate reactions,[20] while Passos and collaborators[18] found 57% of moderate DIs and 33% of severe DIs.

Most medications involved in the DIs are found to be used for pain relief or discomfort. This may be associated with the underlying disease profile and reason for hospitalization of the patients in this study (neoplasia and pain, respectively).

The participation of dipyrone in several interactions agrees with the literature. Similar results were found in Brazilian studies, such as those of Pivatto Júnior et. al.[21], identifying the presence of the drug in 29.3% of the DIs, and Lima,[3] which highlighted the presence of dipyrone among the three most frequent prescriptions (91%).

Similar data were identified by Okuno et. al.,[19] who found an occurrence of an 11.9% interaction between Dipyrone and Enoxaparin. On the other hand, Pivatto Júnior et. al[21] verified the occurrence of the Dipyrone + Furosemide interaction in 2.7% of the prescriptions, being among the 10 most frequent DIs. Pivatto Júnior et. al.[21] found that the Dipyrone + Captopril DI was the most frequent (9.7%). Passos & Gomes Cardoso[18] identified this association in 3.6% of the investigated DIs.

The interaction between dipyrone and captopril is found in both hospital and outpatient settings. The appropriate management for this interaction is monitoring renal function and ensuring that the patient is hydrated, especially if they are elderly.[16]

DIs involving dipyrone should be carefully analyzed, since the risk-benefit ratio of the indicated management must be established. In most cases, the clinical pharmacist alerts the multidisciplinary team about the potential interaction and thus the decision is made jointly, assessing the patient's clinical situation, choosing to change or maintain therapy.

Dipyrone and enoxaparin are medications widely used in hospitals, especially in intensive care. According to Micromedex®[16], the combination of a non-steroidal anti-inflammatory drug (NSAID) and a low molecular weight heparin may increase the risk of bleeding.

The likely mechanism of this interaction may be the reduction of the platelet function or decreased coagulation. As a management technique, dipyrone withdrawal is indicated when possible or, if maintained, continuous patient follow-up tracking for signs of bleeding.[16, 22]

The classification of the level of scientific evidence about an interaction is important to guide the pharmacist when assessing a clinical situation. The level of evidence of most interactions found was considered good or excellent. This result is similar to that found by Bakes,[23] who identified 15% of DIs with excellent documentation. However, it is noteworthy that most severe DIs have only reasonable documentation (59.5%).

The use of databases to check interactions has been ample and contributed to the agility of information. However, some aspects that may overestimate the prevalence of interactions are identified because it is necessary to understand the connection between the potential DIs and the ADRs resulting from the interactions.[15,21] Limitations such as lack of information on clinical protocols, lack of dose in the records, in addition to the analysis of drugs in pairs and not as a whole and the impossibility of entering patient data in the application interfere with this process.[15,21] Another important point is the discrepancy between commercially available databases.[15]

In this study, it was not possible to follow up the patients to confirm the predicted effect of the DIs due to the short time period and the limited number of patients. These factors, associated with the fact that the study was carried out in a single hospital unit, are the main limitations of the study, requiring caution in extrapolating its results.

Conclusion

From this study it was possible to trace the profile of most prescribed drugs at the time of medical admission, with emphasis on analgesics, especially dipyrone. It was possible to observe the complexity of the DIs found, many severe and most with a good level of evidence.

The results point to the importance of the analysis of DIs in the care process that must be performed by the Pharmacy Service with the patient and with the multidisciplinary team, exercising the concept of transversality and welcoming, addressed in the National Humanization Policy.[24]

In this context, it is important to highlight the presence of the pharmacist at the time of patient admission to contribute to the prevention of adverse events related to medications, as well as to act in drug conciliation with the multiprofessional team.

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Conflict of Interest

The authors declare no conflicts of interest.

Contributors

JLS, SRC and LRS full content; JLS and SRC research project design and planning; JSL and SRC data acquisition; JLS and SRC data analysis and interpretation; JLS, SRC and LRS writing and critical review; JLS, SRC and LRS guarantee of the accuracy and integrity of any part of the work.

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