Abstract

Introduction: In clinical practice, drug 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
Introduction

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

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

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. When detected, DIs may be subjected to pharmaceutical intervention to optimize drug therapy.

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.

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. 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.

During hospitalization other medications that were not part of the previous therapy may be prescribed. Changing care levels for the pharmacotherapeutic follow-up of patients.

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.

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 inpatients and outpatients. According to the institutional survey, the average outpatient collection took place between September and November 2017.

The 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 CAEE 67114817.9.0000.5245 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>
<thead>
<tr>
<th>Characteristic</th>
<th>Descriptive statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years old) mean (SD)</td>
<td>59.98 (XXXX)</td>
</tr>
<tr>
<td>Gender n (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>73 (41.2)</td>
</tr>
<tr>
<td>Male</td>
<td>104 (58.8)</td>
</tr>
<tr>
<td>Previous disease n (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>171 (96.6)</td>
</tr>
<tr>
<td>No</td>
<td>6 (3.4)</td>
</tr>
</tbody>
</table>

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 dyspepsia (5.0%), encephalopathy (3.9%), POAD, liver, urinary tract infection (UTI) and other procedures (3.4%), amputation, diarrhea, infected lesion and sepsis (2.8%), compensated DM and weight loss (2.6%), compensation, dehydration, arteriovenous fistula (AVF) failure, hypertension, hematuria, pneumonia, cough, deep vein thrombosis (DVT) and vomiting (1.7%), anasarca, abscess, tiredness, cinchosis, convulsion, compensated COPD, cancer staging, hypoxemia, compensated 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 Micromedx® 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%), ciprofloxacin (12.7%), tramadol (11.7%), ondansetron (8%), esparoxil (7.1%), 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.

From the Micromedx® 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.

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. In this work, all levels of classification were adopted.
Table 2: ATC classification of the 10 drugs in most interactions.
Río de Janeiro, 2017; N=600 interactions

<table>
<thead>
<tr>
<th>Medication</th>
<th>ATC</th>
<th>n Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dipyrone</td>
<td>N02BB02</td>
<td>209 (43.8)</td>
</tr>
<tr>
<td>Bromopride</td>
<td>A03FA04</td>
<td>110 (18.3)</td>
</tr>
<tr>
<td>Captopril</td>
<td>C09AA01</td>
<td>73 (12.7)</td>
</tr>
<tr>
<td>Tramadol</td>
<td>N02AX02</td>
<td>67 (11.7)</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>A04AA01</td>
<td>48 (8.0)</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>B01AB05</td>
<td>43 (7.1)</td>
</tr>
<tr>
<td>Losartan</td>
<td>C09CA01</td>
<td>42 (7.0)</td>
</tr>
<tr>
<td>AAS</td>
<td>B01AC06</td>
<td>41 (6.8)</td>
</tr>
<tr>
<td>Regular Insulin</td>
<td>A10AB01</td>
<td>41 (6.8)</td>
</tr>
<tr>
<td>Morphine</td>
<td>N02AA01</td>
<td>39 (6.5)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Interaction Type</th>
<th>Documentation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>Good</td>
</tr>
<tr>
<td>Severe</td>
<td>23 (6.4%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>53 (23.1%)</td>
</tr>
<tr>
<td>Mild</td>
<td>0</td>
</tr>
<tr>
<td>Contraindicated</td>
<td>0</td>
</tr>
</tbody>
</table>

Discussion

The mean age observed is similar to that observed by Vonbach et al., males prevailing with 53%. In similar studies, Passos et al. and Okuno et al. 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. where 62% of the observed interactions are of unknown and moderate upon admission. A North American study found 43.6% of severe and 33% of moderate reactions, while Passos and collaborators 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 Junior et al., identifying the presence of the drug in 29.3% of the DIs, and Lima, which highlighted the presence of dipyrone among the three most frequent prescriptions (91%).

Similar data were identified by Okuno et al., who found an occurrence of an 11.9% interaction between Dipyrone and Enoxaparin. On the other hand, Pivatto Junior et al. verified the occurrence of the Dipyrone + Furosemide interaction in 2.7% of the prescriptions, being among the 10 most frequent 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.

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, 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.

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, 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. 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. Another important point is the discrepancy between commercially available databases.
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.

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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I declare that the research did not receive funding for its accomplishment.

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, JLS 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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References