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Potential drug-drug interactions in a Brazilian teaching hospital: age-related differences?

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ABSTRACT

This study proposes to measure frequency and to characterize the profile of potential drug interactions (pDDI) in a general medicine ward of a teaching hospital. Data about identification and clinical status of patients were extracted from medical records between March to August 2006. The occurrence of pDDI was analyzed using the database monographs Micromedex® DrugReax® System. From 5,336 prescriptions with two or more drugs, 3,097 (58.0%) contained pDDI. The frequency of major and well document pDDI was 26.5%. Among 647 patients, 432 (66.8%) were exposed to at least one pDDI and 283 (43.7%) to major pDDI. The multivariate analysis identified that factors related to higher rates of major pDDI were the same age (p< 0.0001), length of stay (p< 0.0001), prevalence of hypertension [OR=3.42 (p< 0.0001)] and diabetes mellitus [OR=2.1 (p< 0.0001)], cardiovascular diseases (p< 0.0001) and the number of prescribed drugs (Spearman's correlation=0.640622, p< 0.0001). Between major pDDI, the main risk was hemorrhage (50.3%), the most frequent major pDDI involved combination of anticoagulants and antiplatelet drugs. Among moderate pDDI, 3,866 (90.8%) involved medicines for the treatment of chronic non-communicable diseases, mainly hypertension. In HU-USP, the profile of pDDI was similar among adults and elderly (the most frequent pDDI and major pDDI were same), the difference was only the frequency in either group. The efforts of the clinical pharmacists should be directed to elderly patients with cardiovascular compromise, mainly in use of anticoagulants and antiplatelet drugs. Furthermore, hospital managers should increase the integration between levels of health care to promote safety patient after discharge.

Keywords: Drug interactions. Aged. Internal Medicine. Hospitals, University.

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INTRODUCTION

The proportion of elderly in the world population has increased because of

improvement of sanitary conditions, quality of life and technological advances in health. By 2025 it is estimated that Brazil will have the sixth largest elderly population in the world (OMS, 2005). With population aging around the world, it has been increasing the prevalence of chronic diseases. The complexity of these diseases and the polypharmacy leads to high numbers of potential drug-drug interactions (Marengoni *et al*., 2011; Pasina *et al*., 2013). Furthermore, the severity of events tends to be higher upon age-related physiological changes and altered pharmacokinetic and pharmacodynamics (Maher *et al*., 2014).

It is well known that elderly patients exhibit high risk of adverse drug events. In this population, the odd of being hospitalized for adverse drug reactions or adverse drug events is four to seven times higher than younger people (Budnitz *et al*., 2006; Carrasco-Garrido *et al*., 2010; Leendertse *et al*., 2010; Pirmohamed *et al*., 2004).

It is estimated that one in two hundred patients hospitalized in the U.S. has a serious adverse event due to drug-drug interactions, moreover one in ten thousand deaths in the hospital can be attributed to these interactions (Fuhr, 2008). A recently published systematic review suggests that 1.1% of hospital admissions are due to drug-drug interactions (Dechanont *et al*., 2014). A large prospective observational study shown that 1% of all hospital admissions are due to drug-drug interactions (Pirmohamed *et al*., 2004), regarding the elderly population this proportion can be higher than 4.8% (Becker *et al*., 2007).

Despite the low proportion of ADE related to drug interactions, it is important to consider these events are avoidable. The adoption of an electronic prescription drug-monitoring program with clinical decision support can significantly reduce the occurrence of adverse drug events, improving quality and efficiency of drug treatment (Jano

& Aparasu, 2007). However, researchers still have shown that physicians ignore the drug-drug interaction alerts. One of the main reasons for that is the lack of objective information about the clinical relevance of drug interactions and their consequences (Payne *et al*., 2015; Smithburger *et al*., 2011).

The majority of studies on drug-drug interactions subject describe specific drug interactions or therapeutic classes, frequency or risk factors for drug interactions. Medicine utilization and pDDI prevalence studies are a powerful tool for healthcare administration entities.

It is widely accepted that prevalence of potential DDIs in geriatric patients may vary according to the design of the study, the clinical setting, database and the severity of DDIs. It is also known about the importance to identify and understand the differences in the frequency and profile of the potential drug interactions at healthcare services to plan appropriate interventions, if necessary.

This study aimed to verify the pDDI in a general medicine ward of well-established public teaching hospital with clinical pharmacy service and to evaluate if the pDDI profile was different according to age group (adults and elderly).

METHODS

A transversal and observational study was conducted during 6 months in a general medicine ward of a Brazilian teaching hospital – Hospital Universitário da Universidade de São Paulo (HU-USP) (São Paulo University Hospital), in São Paulo, Brazil. This 256-bed public teaching hospital offers a medium-complexity clinical service to university students and the local population.

Between March 1, 2006 and August 31, 2006 all admissions (712) at the 44-bed adult internal medicine ward were followed, comprising a total of 8,371 drug orders. The Pharmacy Service is centralized and attends all inpatients prescription. Every ward has a clinical pharmacist who is responsible for reviewing all prescriptions. Drugs are dispensed to patients, for a maximum period of 8 hours.

Exclusion criteria were patients under 18 years of age, patients without prescription drug, hospital stay less than 24 hours, transferred other ward or hospital and those for which the data were incomplete. Patients transferred were excluded because the study objective was to evaluate the profile of the interactions during hospitalization specifically in the internal medicine unit.

From medical records were collected the following data: date, patient identification (name, age and gender), prevalence of hypertension and diabetes mellitus. After discharge the primary diagnosis (according to ICD-10 classification) were listed as described in the discharge summary, and length of stay. All patients ≥60 years of age were classified as 'elderly population'.

Only the drugs prescribed and administered to the patient were considered to the drug-drug interaction analyses (the signature of a head nurse confirmed that the drug was administered to the patient). Daily prescription included all drugs administered during 24 hour of hospitalization, regardless if they were prescribed at one time or by means of additional prescription. It was not differentiate the drugs route, frequency of administration and presentation. The drugs were classified using the Anatomical Therapeutic Chemical Classification (ATC).

Orders with two or more drugs were evaluated in relation to potential drug interactions. A potential drug interaction was defined as an occurrence in which 2 drugs known to interact were concurrently prescribed and administered, regardless of whether adverse events occurred. These pDDI were determined and classified employing the software Micromedex DrugReax® System (Micromedex, 2014), according severity (major, moderate and minor), documentation (excellent, good, fair, poor or unlikely). Drug interactions sorted as poor or unlikely documentation were not included.

Every pDDI found were listed and analyzed regarding it monograph which contains information on monitoring, management, severity, probable mechanism and risk. Based on the monographs, drug interactions were classified according to the probable mechanism (pharmacological, pharmacokinetic or pharmaceutical), risk and severity.

All pDDI during hospitalization were identified, to measure pDDI cumulative incidence between patients (numerator = total number of patients exposed to at least one pDDI; denominator = total number of patients); major pDDI cumulative incidence and moderate pDDI cumulative incidence. In addition, we calculated pDDI cumulative incidence in orders (numerator = total number of orders with at least one pDDI; denominator = total number of orders); major pDDI cumulative incidence in orders and moderate pDDI cumulative incidence in orders.

Patient's bio demographical data and other prescription data were presented as mean, median, standard deviation and percentage, using Microsoft Excel ® version 2007. The Shapiro-Wilks test was used to verify the normality of the data. It were employed the Wilcoxon Sum of Ranks test, Fisher's exact test, chi-square and Student's t-test in statistical analysis. It was applied multivariate logistic regression analysis to determine the factors associated with exposure to pDDI and major pDDI which is the dependent variable (Yes / No) and using as independent variables age, gender, comorbidities (hypertension and diabetes), the number of medications, and length of stay. The confidence level adopted for all tests was 95%.

The research project was approved by the local ethics committee and registered in the National System of Information on Ethics in Research (SISNEP; CAAE no 0024.0198.018-07).

RESULTS

From 712 patients admitted at the internal medicine

ward of the HU-USP in the studied period, 647 (91%) were included, accounting 5,666 orders. Sixty-five patients were excluded due to: 4 (0.6%) under 18 years old, 19 (2.7%) transferred, 28 (4%) discharged in less than 24 hours and 14 (2%) received no medicines.

The mean age among patients was 56.7 ± 19.8 (range 18 to 96) years and the medium length of hospital stay were 10.7 days. Patients were divided between adults (331; 51.2%) and elderly (316; 48.8%). Table 1 describes demographic and clinical characteristics for both groups.

It was prescribed 219 different drugs, classified into 13 different anatomical groups according to ATC. Five anatomical groups were most frequently prescribed, accumulating 82.9% of all 31,730 prescribed drugs (Table 1), considering all patients.

Drug orders with two or more prescribed drugs (5,336) were considered for the analysis of pDDI and major pDDI frequency. Among these orders, 3,097 (58.0%) had at least one pDDI and 1,414 (26.5%) presented at least one major pDDI. Of the 219 drugs prescribed, 10 (4.6%) could not be analyzed because they were not included in the database Micromedex DrugReax® System, they are benserazide, bromopride, cloxazolam, etoricoxib, fenoterol, lanatosídeo C, levomepromazine, metamizole, pericyazine and salbutamol.

The multivariate analysis identified factors related to higher rates of potential drug interactions and potential major drug interactions between prescriptions studied as: age ($p<0.0001$), length of stay ($p<0.0001$), prevalence of hypertension ($p<0.0001$) and diabetes mellitus ($p<0.0001$), cardiovascular diseases ($p<0.0001$) and the number of prescribed drugs. Patients with hypertension and diabetes had, respectively, 4.93 and 2.79 more chance of pDDI, and 3.42 and 2.1 more chance of prescriptions with major pDDI. There was no association between gender and the occurrence of pDDI or major pDDI.

Applying the chi-frame Cochran-Mantel-Haeszele Spearman's correlation, the association between the number of drugs prescribed and the pDDI was confirmed in both groups: adults ($p <0.0001$, correlation coefficient =0.652148) and elderly ($p <0.0001$, correlation coefficient =0.646153). A high number of elderly patients were exposed to pDDI (OR 2.8); major pDDI (OR 3.1) and moderate pDDI (OR 2.4), as shown in Table 2.

Table 3 presents the profile of pDDI according documentation, severity, associated risk and management

Table 1 - Demographic and clinical characteristics of patients during hospitalization in HU-USP, between March and August 2006

	Adult	**Elderly**	**p**
Total number of patients	**331**	**316**	
Gender, n (%)			
Male	195 (58.9%)	154 (48.7%)	0.012[a]
Female	136 (41.1%)	162 (51.3%)	
Hypertension, n (%)	92 (28.0%)	164 (51.9%)	<0.000[b]
Diabetes, n (%)	54 (16.3%)	67 (21.2%)	0.054[b]
Average length of stay± SD, days	9.65±9.06	11.61±9.57	0.000[a]
Average age ± SD, years	40.57±12.35	73.70±8.59	----
The most frequent discharge diagnoses, n (%)			
Bronchopneumonia	65 (19.6%)	73 (23.1%)	0.282[a]
Acute myocardial infarction	15 (4.5%)	43 (13.6%)	0.000[a]
Cerebrovascular accident	12 (3.6%)	15 (4.7%)	0.476[a]
Congestive heart failure	7 (2.1%)	11 (3.5%)	0.291[a]
Total number of prescriptions	**2712**	**2954**	
Average number of drugs prescribed ± SD	5.20±2.85	6.25±2.82	<0.000[c]
The most frequently prescribed ATC groups, n (%)			
Cardiovascular system - C	439 (16.2%)	750 (25.4%)	0.006[a]
Alimentary tract and metabolism - A	521 (19.2%)	473 (16.0%)	<0.000[a]
Nervous System - N	504 (18.6%)	387 (13.1%)	<0.000[a]
Blood and Blood forming organs -B	336 (12.4%)	508 (17.2%)	<0.000[a]
Antiinfectives for systemic use - J	328 (12.1%)	458 (15.5%)	<0.000[a]
The most frequently prescribed individual drugs, n (%)			
Heparin	608 (22.4%)	1,262 (42.7%)	<0.000[a]
Captopril	242 (8.9%)	1,103 (37.3%)	<0.000[a]
Metamizole	877 (32.3%)	700 (23.7%)	<0.000[a]
Acetylsalicylic acid	652 (24.0%)	1,031 (34.9%)	<0.000[a]
Omeprazole	464 (17.1%)	762 (25.8%)	<0.000[a]

Legend: SD = Standard deviation; [a]=chi-square test; [b]=fisher's exact test ; [c]= Student's t-test

Table 2 – Patients exposed, frequency and number of potential drug interactions in orders of patients during hospitalization in HU-USP, between March and August 2006

	Adult	**Elderly**	**p**
Total number of patients	**331**	**316**	
Exposed at least one pDDI, n (%)	187 (56.5%)	247 (78.2%)	<0.001[a]
Exposed at least one major pDDI, n (%)	82 (24.8%)	159 (50.3%)	<0.001[a]
Exposed at least one moderate pDDI, n (%)	148 (44.7%)	210 (66.4%)	<0.008[a]
Average number of pDDI ± SD	1.48±2.24	2.22±2.66	<0.001[a]
Average number of major pDDI ± SD	0.61±0.98	0.68±0.92	<0.001[a]

Legend: SD = Standard deviation – [a]=chi-square test

Table 3 – Profile of potential drug interactions in orders of patients in general medicine ward of HU-USP, between March and August 2006

Severity of potential drug interactions			
Major pDDI		1,940 (19.5%)	
Moderate pDDI		4,259 (42.8%)	
Total of pDDI		**9,951 (100.0%)**	
Associated risk of potential drug interactions clinically relevant			
Major pDDI		**Moderate pDDI**	
Hemorrhage	976 (50.3%)	Hypertension	1,166 (27.4%)
Hyperkalemia	211 (10.9%)	Hypotension	747 (17.5%)
Myopathy / Rhabdomyolysis	132 (6.8%)	Hemorrhage	459 (10.8%)
Cardiotoxicity	91 (4.7%)	Loss / reduction of the effect	398 (9.3%)
Respiratory depression	87 (4.5%)	Cardiotoxicity	243 (5.7%)
QT prolongation	58 (3.0%)	Hypo/Hyperglicemy	228 (5.4%)
Digitalis intoxication	58 (3.0%)	SNC depression	175 (4.1%)
Others	327 (16.9%)	Others	843 (19.8%)
TOTAL	**1,940 (100.0%)**	**TOTAL**	**4,259 (100.0%)**
Management strategies for potential drug interactions clinically relevant			
Major pDDI		**Moderate pDDI**	
Avoid/ Monitor signs and symptoms	1,089 (56.1%)	Avoid/ Monitor signs and symptoms	1,931 (45.3%)
Monitor signs and symptoms	328 (16.9%)	Monitor signs and symptoms	1,718 (40.3%)
Dose adjustment	224 (11.5%)	Dose adjustment	259 (6.1%)
Avoid	212 (10.9%)	Avoid	141 (3.3%)
Use with caution	76 (3.9%)	Use with caution	112 (2.6%)
Others	11 (0.6%)	Others	285 (6.7%)
TOTAL	**1,931 (45.3%)**	**TOTAL**	**4,259 (100.0%)**

Table 4 – Profile of ten more frequent major and well-documented potential drug-drug interactions, which patients were exposed during hospitalization in HU-USP, between March and August 2006

Drug	**Drug**	**Total**	**Adult**	**Elderly**	**p**
		N (%)	**N (%)**	**N (%)**	
Anticoagulants or antiplatelet drugs	Any drug	214 (33.1%)	58 (17.5%)	156 (49.4%)	<0.000[a]
Anticoagulant	Antiplatelet	142 (21.9%)	32 (9.7%)	110 (34.8%)	<0.000[a]
Aspirin	Heparin	112 (17.3%)	21 (6.3%)	91 (28.8%)	<0.000[a]
Clopidogrel	Omeprazole	25 (3.9%)	9 (2.7%)	16 (5.1%)	0.122[a]
Captopril	Spironolacton	23 (3.6%)	11 (3.3%)	12 (3.8%)	0.745[a]
Captopril	Potassium chloride	18 (2.8%)	12 (3.6%)	6 (1.9%)	0.182[a]
Aspirin	Warfarin	14 (2.2%)	0 (0.0%)	14 (4.4%)	0.000[a]
Ciprofloxacyn	Insulin	13 (2.0%)	6 (1.8%)	7 (2.2%)	0.715[a]
Simvastatin	Warfarin	12 (1.8%)	3 (0.9%)	9 (0.9%)	0.067[a]
Heparin	Warfarin	11 (1.7%)	4 (1.2%)	7 (2.2%)	0.322[a]

Legend: [a]=chi-square test

strategies. It was observed that 2,726 (51.1%) of orders presents at least one clinically relevant pDDI (major or moderate interaction), accounting 6,199 (62.3%). Between major pDDI, the main risk identified was hemorrhagic events (50.3%).

The ten more frequent major (potential) drug-drug interactions

which patients were exposed are shown in Table 4. Among moderate pDDI, 3,866 (90.8%) involved medicines for the treatment of chronic non-communicable diseases, mainly hypertension (74.9%).

Only 7 (0.1%) of the all interactions were due to pharmaceutical interaction (incompatibility). Most of drug interactions identified were related to pharmacodynamics (5,532, 55.6%) and pharmacokinetic (3,426; 34.4%).

DISCUSSION

The mean age of the patients (56.7 ± 19.8 years) was consistent with the data reported in a study conducted at a university hospital in Paraná (Brazil), with similar characteristics to HU-USP (52.7 ± 18.9 years). The high proportion of men, inclusion of surgical wards and patients aged 12 to 17 years can explain the slight difference in the mean age (Cruciol-Souza & Thomson, 2006). Despite bronchopneumonia have been the most common diagnostic (study was conducted during the winter), the internal medicine ward in HU-USP revealed a care profile similar to cardiac units.

Cardiovascular diseases are very common in the population and are responsible for a substantial portion of hospital admissions in Brazilian hospitals, followed by respiratory diseases - considering no obstetrical admissions (Brazil, 2013). Acute myocardial infarction also is appointed as a frequent cause of hospitalization in the literature (Cruciol-Souza & Thomson, 2006; Moura *et al*., 2009; Reis & Cassiani, 2011).

The average number of prescribed drugs was lower than the data reported in another Brazilian study (7 drugs per prescription) whose hospital had the same characteristics as the HU-USP, which can be explained by the fact that they were included only drugs actually administered to the patients and not just prescribed (Cruciol-Souza & Thomson, 2006). In Brazil there is the practice of prescribing drugs on a demand schedule ("when necessary"), especially in the cases of pain, fever, nausea and vomiting. The more frequent anatomical groups coincide with those described as the most prescribed in other Brazilian studies, both in hospital wards (Cruciol-Souza & Thomson, 2006), as in intensive care units (Carvalho *et al*., 2013; Lima & Cassiani, 2009; Reis & Cassiani, 2011), changing only the order in which they appear.

Like in others studies, it was observed that elderly had hospital length of stay longer and high prevalence of cardiovascular disease and hypertension (Egger *et al*., 2003; Pasina *et al*., 2013), although there was no difference between the groups regarding the prevalence of diabetes.

Both frequencies of pDDI and major pDDI were higher than that observed in other Brazilian and international studies, although it was expected a low frequency since we have considered only the medicines effectively administered (Ahmad *et al*., 2015; Ismail *et al*., 2013; Moura *et al*., 2009; Cruciol-Souza & Thomson, 2006). A challenge for comparison was the lack of internal medicine ward studies in hospitals with similar characteristics to the HU-USP and same drug interaction database (Micromedex®). Similar conditions were only observed in the study of Cruciol-Souza and Thomson (2006), which reported that 49.7% of 1785 prescriptions reviewed exhibited at least one drug-drug interaction (Cruciol-Souza & Thomson, 2006). This difference could be related to the great frequency of cardiovascular disease among patients and large elderly hospitalization rate (48.8%), higher than observed among adult patients hospitalized in Brazilian hospitals (40%) and the state of São Paulo (41%) (Brazil, 2013). Recently, a systematic review reported that the prevalence of patients with drug interactions and the number of interactions per 100 patients ranged, respectively, from 15% to 45% and from 37 to 106, depending on the group of studies analyzed (Espinosa-Bosch *et al*., 2012). In the same review, the authors confirmed that a large number of studies about drug interactions prevalence in hospitals have a very wide results, depending on the choice of study design and hospital characteristics (Espinosa-Bosch *et al*., 2012). Moreover, the prevalence of pDDI and major pDDI were greatly influenced by the large number of patients exposed to the combined use of anticoagulants and antiplatelet medicines, mainly among elderly ($p<0.0000$).

Age, length of stay and the number of prescribed drugs are some of the drug interaction risk factors found in our study that were previously observed in other studies (Cruciol-Souza & Thomson, 2006; Hammes *et al*., 2008; Moura *et al*., 2011). Nonetheless cardiovascular diseases have already been reported in some studies as an important predictor of drug interactions (Cruciol-Souza & Thomson, 2006; Pasina *et al*., 2013; Reis & Cassiani, 2011). We did not notice association between gender and general pDDI or major pDDI occurrence as described in systematic review (Alhawassi *et al*, 2014).

Circulatory system diseases are the leading cause of morbidity and mortality, and its major risk factors are hypertension and diabetes. It was expected that patients with hypertension and diabetes would be more exposed to the risk of pDDI. Recent review about drug-drug interactions prevalence was higher in elderly patients as well as in patients with heart diseases (Espinosa-Bosch *et al*., 2012).

Despite the high pDDI and major pDDI prevalence, it was expected these data in a hospital setting. Although potential risk, they cannot be considered medication errors or contra-indicated. In fact, most associations are routinely used for better therapeutic results, and it requires only patient monitoring. In this study, hemorrhage (23.2%) and hypertension (17.2%) was found potential adverse drug

events. This data are in accordance to previously study reported in Brazil (Cruciol-Souza & Thomson, 2006).

Major pDDI profile was largely influenced by the frequency of pDDI observed between elderly patients admitted in this unit, as expected. About a third of all patients (214; 33.1%) were exposed to at least one major pDDI involving anticoagulants or antiplatelet drugs. The use of these medicines among patients subject to preventable adverse drug events and pDDI has been reported in other studies (Alhawassi *et al*, 2014; Dechanont *et al*., 2014; Kongkaew *et al*., 2013; Pirmohamed *et al*., 2004; Salvi *et al*., 2012).

The association of an antiplatelet and an anticoagulant drugs such as "aspirin and heparin" may be recommended in various situations as for the management of conditions such as myocardial infarction with ST-segment elevation, atrial fibrillation and after cardiac revascularization, according European Society of Cardiology guidelines (Camm *et al*., 2012; Steg *et al*., 2012; Windecker *et al*., 2014). Available evidence is not conclusive about the risk and benefit of combination anticoagulant and antiplatelet medicines in the reduction of cardiovascular events; i.e. there is no consensus about damage of combined use (Lane *et al*., 2013; Massel & Little, 2013).

There is considerable debate about the negative impact of the combined use of proton pump inhibitor (PPI) with clopidogrel, one of more observed major pDDI. Recently published reviews concluded that platelet function studies do not demonstrate a consistent interaction between clopidogrel and PPI. Until now studies have failed in determining the risk of an adverse cardiovascular effect due to their heterogeneities in relation to sample and methodology (Focks *et al*., 2013; Kwok & Loke, 2012).

Concomitant use of captopril and spironolactone or potassium supplements is one of the most frequently major pDDI described in outpatients and inpatients (Obreli Neto *et al*., 2012). This drug interaction has been large described in the literature: most frequent in Cruciol-Souza and Thomson (2006) study; second most common among elderly outpatients when evaluated the occurrence of adverse events associated with pDDI (Obreli Neto *et al*., 2012); and classified as a relevant drug interaction in other studies (Hines & Murphy, 2011; Pasina *et al*., 2013). Although it may increase the risk of arrhythmias, this interaction is safe in the hospital setting where potassium test is part of the routine laboratory monitoring. Activity developed with the participation of clinical pharmacists who monitor daily the results of laboratory tests and clinical outcome with the multidisciplinary team.

Moderate pDDI included many interactions between antihypertensive and hypoglycemic medicines, what may explain the high frequency of pharmacodynamics interactions (56.0%) which comprises such clinical effects: hypertension, hypotension, loss/reduction of the effect and hypo/hyperglycemia. Besides, moderate interactions could also mask the use of these interactions to benefit the patient, such as the association between ACE inhibitors and thiazide diuretics to potentiate the antihypertensive effect, for example.

It was observed low proportion of pharmaceutical drug-drug interactions (0.1%), when compared to another Brazilian study in a hospital with similar characteristics where they had a frequency of 14.3% (Cruciol-Souza & Thomson, 2006). We hypothesized that our results are consequences of a well-established clinical pharmacist service provided in the HU-USP, which unfortunately is not a reality in most of Brazilian hospitals (de Castro & Correr, 2007).

Limitations of this study are: clinical manifestations of the pDDIs could not be evaluated; the use of software to identify potential interactions - drug interaction screening software typically produces strong signal levels that can indicate a greater prevalence of pDDI; lack of similar studies to compare and analyze our results.

In clinical practice there is excess of information, which complicates the searching, selection and synthesis to know how to decide about the best therapeutic management. The risk/balance benefit associated with use of a particular medication or drug combinations is a critical step in the decision to use pharmacotherapy. The ability to identify dangerous and clinical relevant drug interactions is a critical facet in a clinical pharmacy service. Inclusion of medicine experts in an interdisciplinary team have contributed to the clinical therapeutic issues understanding, causing a safer and more effective patients outcomes (Chisholm-Burns *et al*., 2010; Kaboli *et al*., 2006).

For an optimal inpatient care is essential to know the drug interaction profile in the clinical practice context, and the most important profile of the pDDI prevalence. In HU-USP, the profile of pDDI was similar among adults and elderly (the most frequent pDDI and major pDDI were the same), the difference was only the frequency in either group. Clinical pharmacists' efforts should be directed to monitor elderly patients with cardiovascular compromises in use of anticoagulants and antiplatelet drugs in this hospital. Furthermore, higher number of pDDI and major pDDI were associated with medicines broadly used in ambulatory setting, healthcare professionals in different setting levels should be encourage cooperating to each other to improve the safety of patients after discharge.

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RESUMO

Interações medicamentosas potenciais em um hospital escolar brasileiro: diferenças relacionadas à idade?

O estudo tem por objetivo descrever o perfil de interações **medicamentosas potenciais (IMP) na clínica médica de**

um hospital escola. Dados sobre a identificação e estado clínico dos pacientes foram extraídos de prontuários médicos, entre março e agosto de 2006. A ocorrência de IMP foi analisada empregando-se o banco de monografias Micromedex DrugReax® System. Das 5.336 prescrições, 3.097 (58,0%) continham IMP. A frequência de IMP graves e bem documentadas foi de 26,5%. Entre os 647 pacientes, 432 (66,8%) foram expostos a pelo menos uma IMP e 283 (43,7%) uma IMP grave. A análise multivariada identificou que os fatores relacionados a maiores taxas de IMP e IMP graves foram os mesmos: idade (p< 0,0001), tempo de internação (p< 0,0001), prevalência de hipertensão [OR=3,42 (p< 0,0001)] e diabetes mellitus [OR=2,1 (p< 0,0001)] , doenças cardiovasculares (p< 0,0001) e o número de medicamentos prescritos (correlação de Spearman =0,640622, p< 0,0001). Entre as IMP graves, o principal risco foi hemorragia (50,3%) e as IMP graves mais frequentes envolviam a combinação de anticoagulantes e agentes antiplaquetários. Entre as IMP de gravidade moderada, 3.866 (90,8%) envolviam medicamentos para o tratamento de doenças crônicas não transmissíveis, particularmente hipertensão. No HU-USP, o perfil de IMP foi similar entre adultos e idosos (as IMP e IMP graves mais frequentes foram as mesmas), a diferença estava apenas na diferença na frequência em cada um dos grupos. Os esforços dos farmacêuticos clínicos deveriam ser direcionados aos pacientes idosos, com comprometimento cardiovascular, principalmente aqueles em uso de anticoagulantes e fármacos antiplaquetários. Além disso, deve-se aumentar a integração entre os níveis do cuidado a saúde para promover a segurança do paciente após a alta.

Palavras-chave: Interações de Medicamentos. Idoso. Medicina interna. Hospitais Universitários.

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