FREQUENCY AND CHARACTERISTICS OF POTENTIAL DRUG-DRUG INTERACTIONS IDENTIFIED IN PATIENTS HOSPITALIZED AT THE INFECTIOUS DISEASES HOSPITAL OF TIRANA

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Abstract

Potential drug-drug interactions (pDDIs) are a serious and frequent health issue, leading to often preventable and predictable adverse drug reactions and other negative outcomes. The objective of this study was to assess the frequency of potential drug-drug interactions and characterize them in patients hospitalized in an Infectious Diseases hospital in Albania. We conducted a cross sectional study in patients discharged from this hospital in Tirana during the period from October 1, 2011 to December 30, 2011 and their medical files were consulted. The detection of pDDIs among prescribed drugs was performed through the Thompson Micromedex®1.0 program, independently by two pharmacists. 31.4% (56) of all patients included in the study experienced at least one pDDI, most of which were of moderate severity and well documented. Drugs most frequently involved in potential DDIs were NSAIDs (24.5%), fluoroquinolones (22.4%), and aminoglycosides (14.3%). Most prevalent specific risks due to pDDIs were decreased effectiveness or decreased plasma levels of one of the drugs (29.6%), increased response or plasma levels of one of the drugs, with risk of increased toxicity (26.5%) and increased risk for tendon rupture (9.1%). According to the results of this study, pDDIs in Albania are frequent and potentially avoidable. Further divulgation and awareness is needed to prevent harmful or clinically important drug-drug interactions. The utilization of appropriate computer programs, pharmacotherapeutic monitoring of patients and the pharmacist´s presence in the multidisciplinary team are some of the recommended ways for the improvement of hospitalized patients´ treatment.

Keywords: Potential drug-drug interactions, hospitalized patients, Albania

Introduction

When two drugs are administered to a patient, they may act independently, or interact with each other. The interaction may increase or decrease the effects of the involved drugs and sometimes may cause unexpected toxicity, side effects or failure of the pharmacological therapy (Hussar, 2007). As newer and more potent drugs become available, the number of serious drug interactions is likely to increase. In a study conducted in an emergency department, De Paepe, Petrovic, Outtier, Van Maele & Buylaert concluded that clinically relevant interactions were related with older age and number of drugs. Measured frequencies of potential drug-drug interactions (pDDIs) vary considerably in different study settings (healthcare levels), ranging from 11% as recorded by Askari et al. in an intensive care unit to 27.8% by Zwart-van Rijkom et al. in a Dutch university hospital and 63% by Mino-León et al in an internal medicine ward in Mexico city. All authors agree that most of the undesired pDDIs are avoidable and implementation of appropriate clinical decision support systems such as computerized alerts or laboratory monitoring might be helpful to decrease pDDIs and potentially enhance patients´ safety. Various studies have showed that drug-drug interactions were associated with polypharmacy (taking more than five drugs), length of stay and cost of hospitalization (Moura, Acurcio & Belo; Vonbach, Dubied, Beer & Krähenbühl). Better knowledge of significantly important pDDIs, identification and characterization of all factors influencing in pDDIs occurrence is essential to improve prescription of medications and therapeutic management of treatments. Since there are no previous data available regarding this health issue in our country, a structured observational study was performed.

The objective of this study was to assess the frequency of potential drug-drug interactions and characterize them in patients hospitalized in an Infectious Diseases hospital in Albania.

Methods

Study design: Cross sectional study.

Reference population was patients discharged from the University Hospital Center "Mother Teresa" in Tirana during the period from October 1, 2011 to December 30, 2011.

The University Hospital Center "Mother Teresa" provides secondary hospital services to the Tirana region and at the same time serves as a tertiary hospital (about 30% of beds) offering a range of unique specialist services in Albania. This Center gives specialized medical assistance; it serves as the basis for the formation of medical students, doctors, health personnel and also as the basis of scientific research in the health sector (VKM nr. 70, date 15.02.2001 “Status of University Hospitals”).

The Documentation Service provided the information for the period of study. It included unique number of the medical file, age, gender, dates of admission and discharge. We consulted all medical files for this period, excluding those with only one or no drugs prescribed. The detection of potential drug-drug interactions (pDDIs) among prescribed drugs was performed through the Thompson Micromedex®1.0 program.

All prescribed drugs in each medical file were checked and the pDDIs found were recorded by two pharmacists in a blind manner. The profile of pDDIs was evaluated as the percentage of files with at least one pDDI and the number of pDDIs in these files. Also, for the purposes of this study, the drug interactions found were classified in terms of interaction severity and literature documentation. Based on the Thompson Micromedex program, pDDIs were classified in contraindicated, major, moderate and minor, whereas their documentation as excellent, good, fair.

The drugs involved in pDDIs were divided by pharmacological groups to identify which group had a higher frequency of potential interaction between drugs. Also, some of them were evaluated in base of their predictability, according to the literature, by Katzung (2007) *Basic & Clinical Pharmacology*.

We employed Microsoft Excel and StatPlus 2009 for data analysis. A descriptive analysis of the study population characteristics was performed.

Results

One hundred seventy-eight patients (44.4% females), mean age 45.5 +/- 18.4 years (range 0.5-86), were included in the study. Patients received an average of 5.7 drugs (95% CI 5.4-6.1) ranging from 2 to 14 drugs during their hospital stay. Mean length-of-stay of patients hospitalized in the Infectious Diseases Hospital was approximately 6 days. 31.4% (56) of all patients included in the study experienced at least one pDDI (Figure 1).

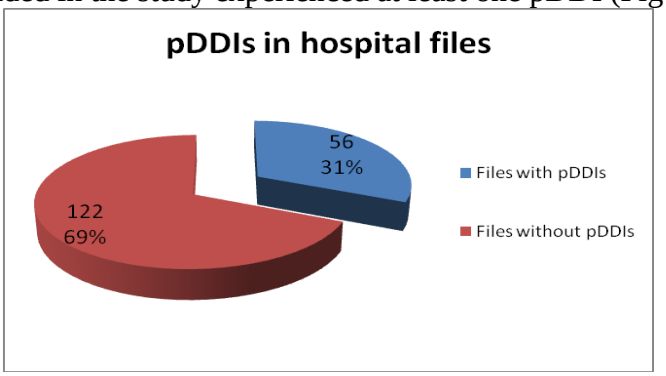

Figure 1. Potential Drug-Drug Interactions identified in the studied hospital files.

Ninety-eight potential interactions between drugs were found in 56 medical files, from which there were 70 different single interactions. The

mean number of pDDIs in these files was 1.75 (range 1-6), SD 1.19. As shown in Figure 2, in the majority of the files (35) only one pDDI was found.

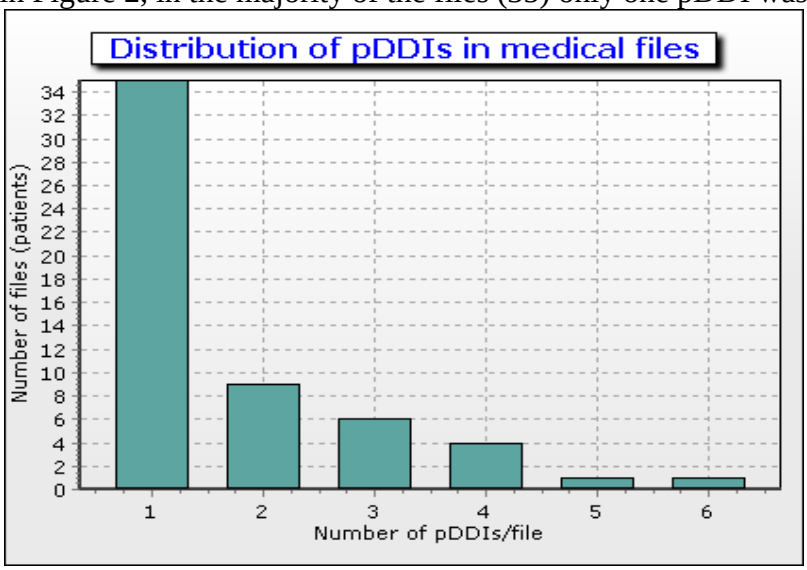

Figure 2. Distribution of pDDIs in medical files

Out of 98 identified pDDIs, most were of moderate and minor severity (65.6% and 16.1%, respectively), shown in Figure 3.

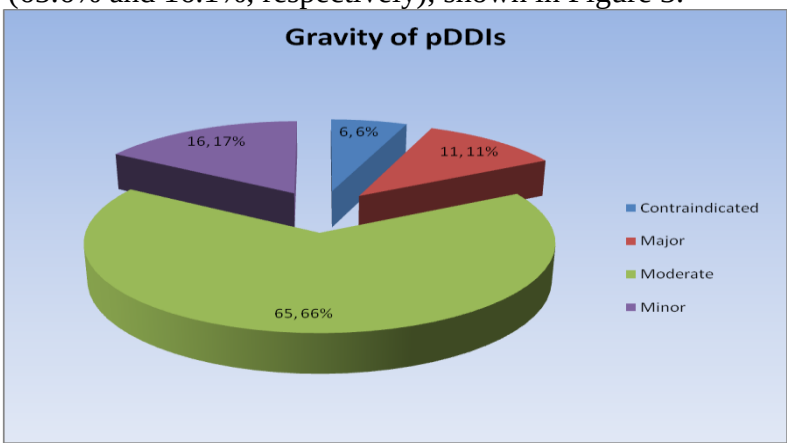

Figure 3. Gravity of pDDIs

Contraindicated - the drugs are contraindicated for concurrent use.

Major - the interaction may be life-threatening and/or require medical intervention to minimize or prevent serious adverse effects.

Moderate - the interaction may result in an exacerbation of the patient's condition and/or require an alteration in therapy.

Minor - the interaction would have limited clinical effects. Manifestations may include an increase in the frequency or severity of side effects but generally would not require a major alteration in therapy.

The literature documentation of these potential DDIs was mainly good (51.5%) and fair (28.2%), represented in Figure 4.

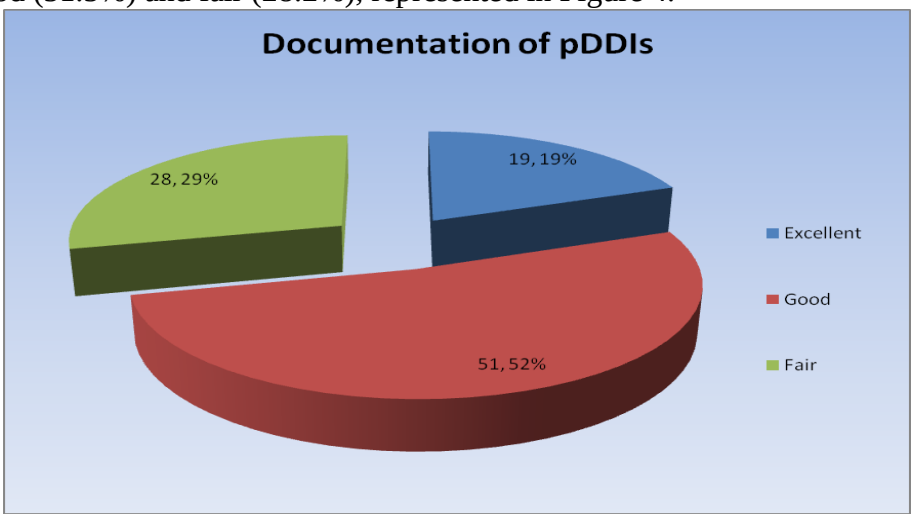

Figure 4. Documentation of pDDIs

Excellent - controlled studies have clearly established the existence of the interaction.

Good - documentation strongly suggests the interaction exists, but well-controlled studies are lacking.

Fair - available documentation is poor, but pharmacologic considerations lead clinicians to suspect the interaction exists; or, documentation is good for a pharmacologically similar drug.

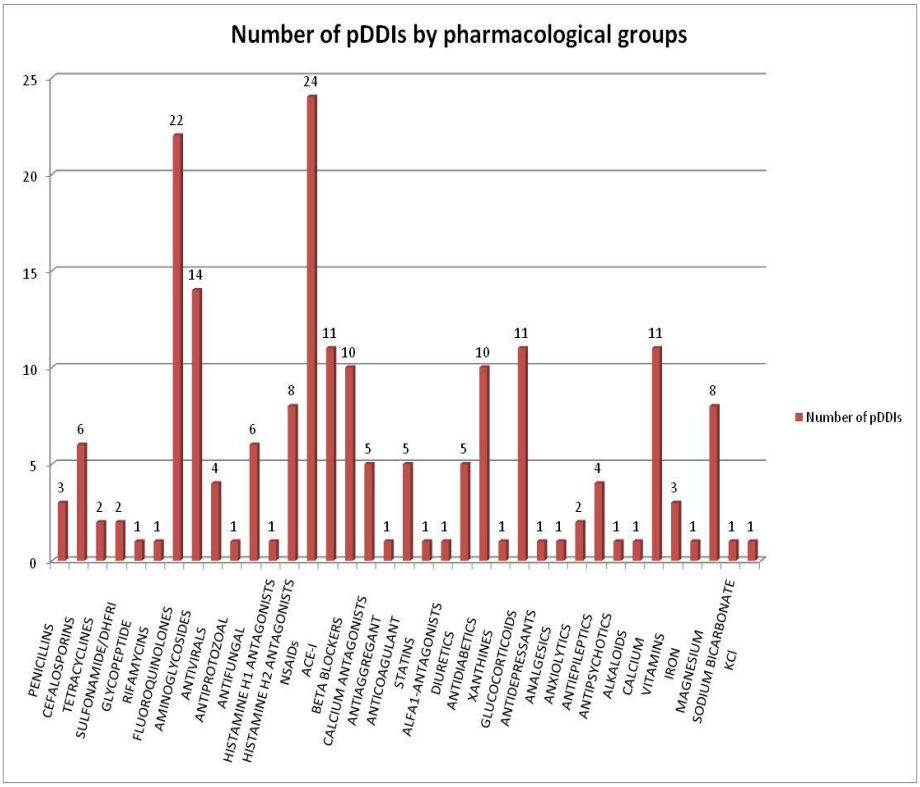

Figure 5. Number of pDDIs by pharmacological group of the drugs involved

Most frequently involved in potential DDIs were non-steroidal anti-inflammatory drugs (24.5%), fluoroquinolones (22.4%), and aminoglycosides (14.3%). Also, frequent pDDIs were found with ACE-Inhibitor drugs (11.2%), glucocorticoids (11.2%), calcium containing products (11.2%), beta-blockers (10.2%) and anti-diabetics (10.2%).

Most prevalent specific risks due to DDI were decreased effectiveness (efficacy) or decreased plasma levels of one of the drugs (29.6%), increased response or plasma levels of one of the drugs, with risk of increased toxicity, (26.5%), increased risk for tendon rupture (9.1%), neuromuscular weakness (8.1%), increased risk of seizures (7.1%).

Figure 6 shows the frequency of different potential drug-drug interactions (interactions that occurred only in one file are not shown).

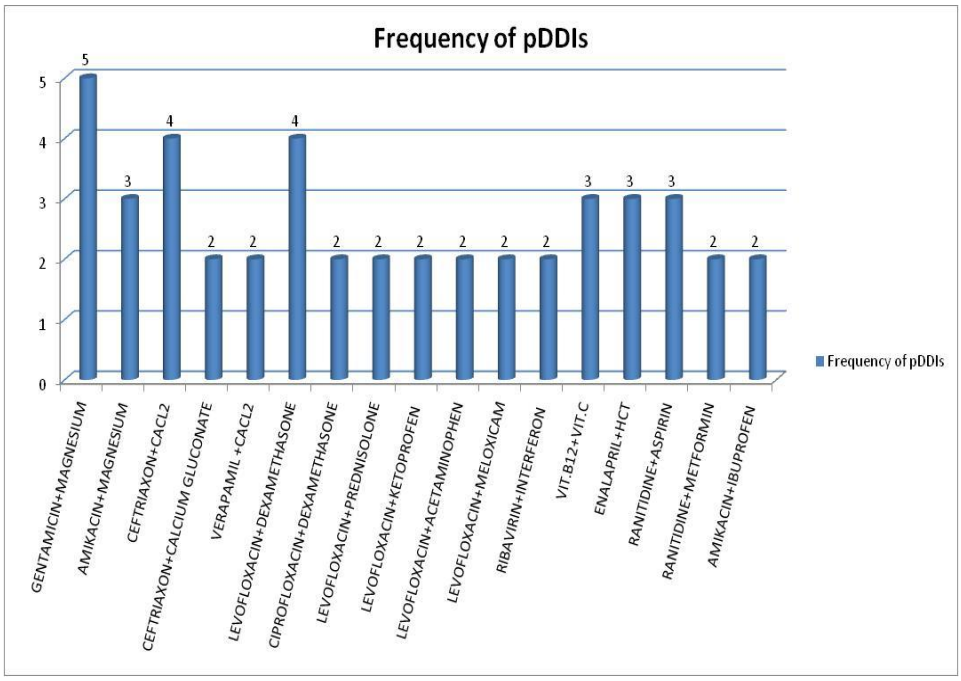

Figure 6. Frequency of potential Drug-Drug Interactions in medical files

According to the literature, some of the pDDIs are highly predictable (ciprofloxacin concurrently with calcium carbonate, doxycycline with calcium chloride), some are predictable (metoprolol with naproxen, enalapril with naproxen, enalapril with aspirin, atenolol with insulin, alfuzosin with bisoprolol, ramipril with ketoprofen), and the others are not predictable or not established.

Highly predictable – the interaction takes place in almost all the patients taking the combination.

Predictable – the interaction takes place in the majority of the patients taking the combination.

Not predictable – the interaction takes place only in some patients taking the combination.

Not established – the data are not sufficient to evaluate the predictability of drug interactions.

Conclusion

It is the first time that a study concerning the profile of drug interactions is conducted in Albania; one of the reasons is the insufficient information about pDDIs and their management in hospitalized patients. According to the results of this study, pDDIs in Albania are frequent and potentially avoidable. Further divulgation and awareness is needed to prevent harmful or clinically important drug-drug interactions. The utilization of

appropriate computer programs, pharmacotherapeutic monitoring of patients and the pharmacist´s presence in the multidisciplinary team are some of the recommended ways for the improvement of hospitalized patients´ treatment.

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