



ORIGINAL ARTICLE

Drug-Drug Interactions Prevalence in Intensive Care Unit Patients of a University Hospital in Iran

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ABSTRACT

Patient's safety is an increasingly recognized challenge. Medicines are primary factor in patient's safety. When the effects and/or toxicity of a drug are affected by another drug is defined as drug-drug interactions (DDIs). Intensive care unit (ICU) patients are especially at increased risk to the development of drug interactions, and this condition is complicated by disease severity and organ failure, both of which can alter the pharmacologic response to medications. The purpose of this study is to evaluate frequency, severity and drug combinations involved in DDIs occurring in a general ICU in Imam Khomeiny hospital ,Urmia university of medical science .This retrospective study included patients who had been hospitalized in the general intensive care unit (GICU) of the hospital over a period of one year. The drugs administered 24 hours after hospitalization, in the GICU, were analyzed to identify potential drug-drug interactions. All possible paired combinations drug-drug were recorded and analysed by using the book Drug Interaction Facts 2010 by David S. Tatro- a book chosen because of its high accuracy when compared to other references. Average number of drugs per encountered was 6.98. 570 DDIs were identified and 91.43% of patients presented with potential drug-drug interactions that 15.09% of them was major in the point of severity. 20.35% of DDIs were highly and 48.42% of them were moderately significant. In the basis of documentation 25.26% of DDIs were established. The most commonly involved medications were ranitidine (220/570), cephalosporins (132/570), dexamethasone (94/570) and phenytoin (82/570). The prevention of DDIs is an important aspect of patient safety. This study such as other studies, showed that potential drug interactions were common in the intensive care unit due to multi- organ involvement , the complexity of the pharmacotherapies administered and multi-drug prescriptions. Therefore, it is imperative that critical care physicians be constantly alert to recognize these problems and provide appropriate mechanisms for therapeutic management. Consultation with clinical pharmacologists, participation of a pharmacologist in clinical rounds, can be mechanisms that results to optimal and rational therapeutic decisions in order to ensure patient safety.

Key words : drug-drug interactions, intensive care unit, clinical pharmacology.

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INTRODUCTION

Health care delivery is not infallible. Errors are common in most health care systems and are reported to be the seventh most common cause of death overall [1]. Patient's safety is an increasingly recognized challenge. Medicines are primary factor in patient's safety. When the effects and/or toxicity of a drug are affected by another drug is defined as drug-drug interactions (DDIs) [2]. Unfortunately, studies focusing on the preventability of adverse drug events (ADEs) have been rare, even though prevention is where efforts must be directed to in order to improve patient safety [3]. Intensive care unit (ICU) patients are specially at increased risk to the development of drug interactions, and this condition is complicated by disease severity and organ failure, both of which can alter the pharmacologic response to medications [4,5] . The number of prescribed drugs is another risk factor for the occurrence of a DDIs. Studies have demonstrated a positive correlation between polypharmacy and DDIs. [6]. It is believed that the potential for drug-drug interaction reaches 100% when the number of drugs prescribed reaches eight [7]. The potential for development of drug-drug interactions increases not only with the number of medications in

use, but also the number of physicians who treat the same patient and older age of patients in ICU are another risk factors that complicate the treatment process [2, 7, 8]. Of studies in this line, a study by Lima et al. in Brazil, indicates that 311 cases of potential drug interactions have been reported in critical care unit patients [2]. The results of another study by Hammes et al. in 2008 also reported higher risk for the occurrence of potential drug interactions in intensive care unit patients [9]. Many studies on medication errors associate the importance of the pharmacist in the multidisciplinary team and during clinical rounds, demonstrating a positive impact of this professional's work in affording a higher quality of health care delivered especially regarding adverse events, inconsistencies in medical prescriptions, and economic impacts [10, 11]. In this regard the purpose of this study is to evaluate frequency, severity and drug combinations involved in DDIs occurring in a general ICU in Imam Khomeiny hospital ,Urmia university of medical science .

METHODS AND MATERIALS

Patients

The present retrospective study was undertaken to determine the prevalence of potential drug-drug interactions and included the patients who had been hospitalized in the general intensive care unit (GICU) of Imam Khomeiny hospital of Urmia. To collect the information, medical records of all patients hospitalized in this ward from 20st March 2012 to 20st March 2013 were evaluated. The participants only included those who were directly transferred to GICU for whom medical records had been established. The number of drugs received by patients in the first 24 hours of hospitalization in ward was extracted from patients' records. Patients' demographic information including age, gender, diagnosis, duration of hospitalization in the ward, and mode of discharge were accessed from medical record.

Data Collecting

To access these information medical records of patients were delivered from Medical Record Department of hospital and recorded in information collecting forms. All possible paired combinations drug-drug were recorded and analysed by using the book Drug Interaction Facts 2010 by David S. Tatro- a book chosen because of its high accuracy when compared to other references [12]. In this book, drugs are sorted based on English alphabet, and type of interactions from the initiation point (abrupt or delayed), intensity (low, medium and high) and possibility (established, probable, suspect, possible, and implausible) is separately specified for each drug. In this study, nutritional supplements, serums, electrolytes and vitamins have not been investigated.

Statistical Analysis

After determination of drug interactions and their mechanisms, data were analyzed by the researchers for all patients in accordance to the study objectives using SPSS18 statistical software by descriptive statistics and the variance analysis.

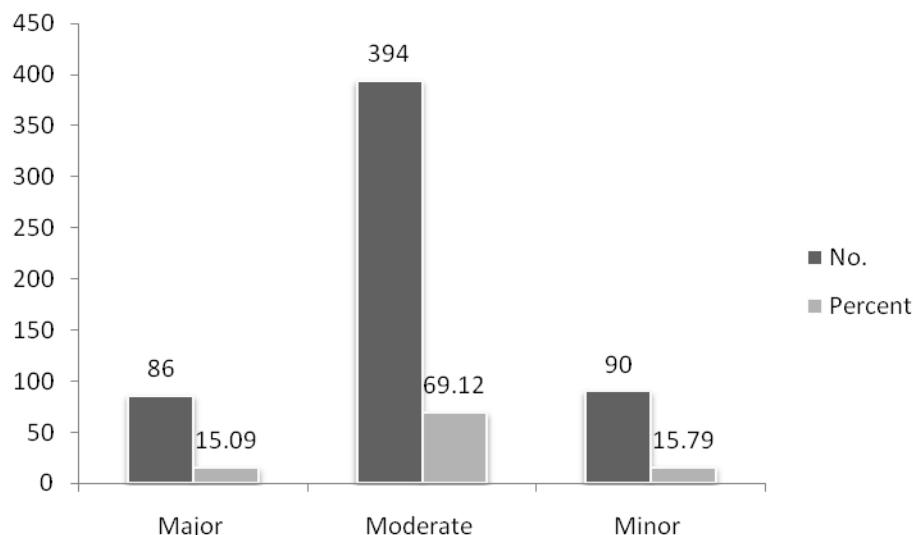
RESULTS

From a total of 210 patients studied, with the mean age of 65.55 years ($SD =23.69$). 64.76% (136) were male and the rest were female. The average ICU stay was 18.05 days ($SD=38.71$). The main reasons for admission in GICU were multiple trauma (27.62%), cerebrovascular accidents (18.1%) and malignancy complications (15.24%). Average number of drugs per encountered was 6.98. In terms of patients discharge from GICU 49% (103) of participants died. 48.2%(101),1.9% (4) and 0.9%(2) of them were respectively discharged following recovery, referred to other hospital and discharged voluntary .(Table-1)

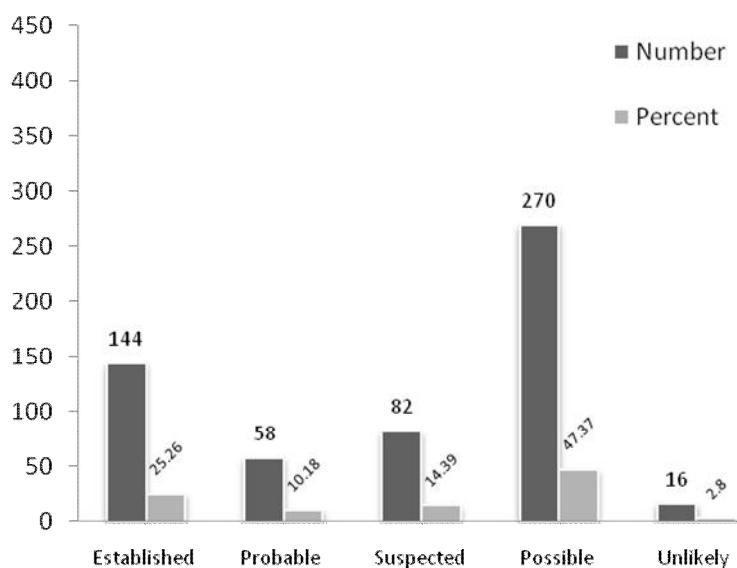
Table-1- Demographic profile of 105 in-patients hospitalized during the period under review

Demographic profile of 105 in-patients hospitalized during the period under review									
Age/Year Mean±SD	Sex		Outcome of hospitalization				Average number of drugs per encounter	average ICU stay ±SD	
65.55 ± 23.69	Male	Female	Died	Discharged	Referred	Voluntary discharge	6.98	18.05 ± 38.71	
	136(64.76)	74(35.24)	103	101	2	4			

570 DDIs were identified and 91.43% of patients presented with potential drug-drug interactions in the first 24 hours of prescription. In terms of initiation, intensity and possibility of drug interactions, delayed, moderate and possible types accounted for the largest percentage of drug interactions respectively. In the point of severity 15.09% (86) of DDIs were major, 69.12% (394) moderate and only 15.79% (90) were minor. (Fig -1)

**Fig-1-Drug-Drug interactions in the point of severity**

In the basis of documentation 25.26% (144) of DDIs were established and 10.18%(58) of them were probable. 47.37% (270) and 14.39% (82) of DDIs were possible and suspected respectively. (Fig-2).

**Fig-2-Drug-Drug interactions in the basis of documentation**

The most commonly involved medications were ranitidine (220/570), cephalosporins (132/570), dexamethasone (94/570) and phenytoin (82/570). (Table-2)

Table-2- The ten most prevalent potential drug interactions

Drug-drug interaction	Significance	Onset	Severity	Documentation	Number	%
Ranitidine + Cephalosporins	4	Rapid	Moderate	Possible	88	15.44
Ranitidine + Dexamethasone	1	Delayed	Moderate	Established	62	10.88
Ranitidine + Phenytoin	4	Delayed	Moderate	Possible	50	8.77
Phenytoin + Dexamethasone	2	Delayed	Moderate	Established	32	5.61
Aminoglycoside + Cephalosporins	2	Delayed	Moderate	Suspected	30	5.26
Ranitidine + Ciprofloxacin	4	Rapid	Moderate	Possible	20	3.51
Aminoglycoside + Vancomycin	4	Delayed	Moderate	Possible	18	3.16
Heparin + Cephalosporins	4	Delayed	Moderate	Possible	14	2.46
Haloperidol + Biperiden	2	Delayed	Moderate	Suspected	8	1.4
Warfarin+ Metronidazole	1	Delayed	Major	Established	4	0.7

DISCUSSION

Several studies have demonstrated high prevalence of drug-drug interactions in critical care unit patients [2,7,9,13,14]. The results of this article are also indicating that the risk of drug-drug interactions among patients in intensive care unit is high. The number of interactions was 570 case, in other words 91.43% of patients presented with potential drug-drug interactions in the first 24 hours of prescription in ICU. An investigation in Brazil reported that on 102 patients hospitalized in critical care unit, the number of potential drug-drug interactions were 311 case that was higher than our results [9]. On the explanation of this finding ,other studies have concluded that the complexity of the pharmaco-therapies administered [14,15], advanced age, number of concomitant drugs, severity of illness, and length of ICU stay [16], causes that intensive care unit patients are at high risk of drug-drug interaction. In terms of initiation and intensity, delayed (67.02%) and moderate (69.12%) types accounted for the largest percentage of drug interactions respectively. These findings are accordance with other studies that revealed more than 59% cases of delayed type of drug interaction in critical care units as well as higher prevalence of moderate types compared to the others [2]. Point of view documentation, possible interaction was 47.37% and 25.26% of interactions were established type. On the explanation of this phenomenon, it can be stated that polypharmacy is the most common cause of DDIs [17] and in our study average number of drugs per encountered was 6.98 that was less than other studies [2,14] but the incidence of DDIs was similar. It seems that training of prescribers and consultant with pharmacologist can reduce the risk of DDIs effectively. The most common interactions observed were associated to ranitidine with cephalosporins (15.44%), ranitidine with dexamethasone (10.88%) and ranitidine with phenytoin (8.77%) which were also the most consumed drugs in critical care units. Another study has similarly pointed to anticonvulsants and stomach acid neutralizers as the most consumed drugs after non-steroidal anti-inflammatory drugs in intensive care units [7]. Since our study has only evaluated the incidence of potential drug -drug interaction in the first 24 hours of hospitalization, it cannot be definitely concluded that whether drug interactions have led to more duration of ICU stay or not; but other investigation showed that the relation between DDIs and duration of staying in ICU was positive [14].

CONCLUSION

Taken together, it can be concluded that the prevalence of potential drug-drug interactions is high in critical care units and is influenced by factors such as complexity of the pharmacotherapies administered, a large number of drugs received by patients, serious and numerous clinical problems, length of ICU stay and advanced age. The majority of potential drug-drug interactions are between drugs that prescribed routinely, so main proportion of potential drug-drug interactions can be decreased by increasing of prescriber's drug information. Physicians should improve and reduce the risks of DDIs with counseling with clinical pharmacologists and participation of pharmacologist in rounds can reduce the rate of interactions.

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