

POTENTIAL DRUG-DRUG INTERACTIONS AMONG HOSPITALIZED ICU PATIENTS

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ABSTRACT

Background: Drug-drug interactions (DDIs) are a major cause for concern in ICU patients due to multiple co-existing conditions and the wide class of drugs they receive. The objective of our study is to identify potential drug-drug interactions among hospitalized ICU patients and to identify the risk factors associated with these interactions. **Methods:** After obtaining approval from Institutional Ethics Committee, a prospective observational study was carried out among 150 ICU patients in Hassan Institute of Medical Sciences attached to Sri Chamarajendra district hospital, HASSAN. As ICU Patients requires stay of more than 24 hour duration were enrolled into the study. The prescriptions were analysed for potential DDIs using MEDSCAPE multidrug interaction checker tool. Descriptive statistics, Students' test, ANOVA and Pearson correlation coefficient were used to analyse the results. **Results:** The incidence of potential DDIs was 98% with 150 prescriptions having at least one potential DDI. A total of 38 potentially interacting drug pairs were identified among which majority were of significant grade while only 3 were serious. Majority of interactions were pharmacodynamic (76.3%) in nature. Aspirin/clopidogrel (71.1%) and pantoprazole/clopidogrel (69.8%) were the most common interacting pairs. Drugs most commonly involved were Aspirin, Clopidogrel, Heparin, Pantoprazole and Ramipril. The potential associated risk factors for drug to drug interactions are related with age, gender, polypharmacy and co-morbid conditions with prolonged hospital stay. **Conclusions:** As all ICU patients need continuous monitoring with proper therapeutic plan. Hence by using the online DDI database will improve the drug therapy and avoid potential interactions leading to adverse effects.

KEYWORDS: DDIs, ICU, MEDSCAPE, Polypharmacy, Risk factors.

INTRODUCTION

Drug-drug interactions (DDIs) represent a special category of adverse drug reactions on concurrent administration of other drugs. Thus either limits therapeutic value or induce toxicity. Overall, 1% of hospital admissions and 16% of admissions due to ADRs can be attributed to DDIs.^[1,2]

Approximately 37 - 60% of patients admitted to hospital may have one or more potential interaction due to drug combinations. In ICU patients, the risk of having potentially interacting drug combinations can additionally increase because of new drugs are often added to the existing drug therapy. DDIs are a concern for patients and providers, as polypharmacy is becoming more common in managing complex diseases or comorbidities and the consequences can range from untoward effects to drug-related morbidity and mortality. Healthcare professional's ability to recognize potential DDIs is important in reducing their potential risks and adverse consequences.^[3]

Studies have revealed that DDIs are a major clinical problem along with other adverse drug reactions especially in the hospitalized ICU patients. The possible reason behind higher DDI rate in ICU patients include elder age, multiple drug regimen, and pharmacokinetic or pharmacodynamic nature of drugs that are used. Hence, this study was conducted to evaluate the pattern of potential drug-drug interactions and to identify the associated risk factors among hospitalized ICU patients in Sri Chamarajendra Hospital.

METHODS**Setting and study design**

After obtaining Institutional Ethics Committee approval, this prospective observational study is carried out in Sri Chamarajendra District Hospital attached to HIMS, HASSAN.

Study population

Patients aged 18 years or older admitted to the ICU unit with a hospital stay of at least 24 hours and those

prescribed two or more drugs were enrolled for the study.

Tools used

Patient case record was used for collecting demographic and medication profile of patients. Computerised DDI database system (MEDSCAPE database) was used to identify and analyse the pattern of potential DDIs. MEDSCAPE contains a separate tool for detecting DDIs known as the multidrug interaction checker tool. On entering the drugs one by one, the program lists the possible DDIs and categorizes DDIs according to their interaction effect, severity (contra-indicated, serious, significant and minor), and management.^[5] A serious interaction emphasizes the need to use an alternative treatment, significant interaction emphasizes the need to monitor the patient closely and minor interactions do not warrant any change in drug therapy.

Operational modality

The medications taken by the patients during their hospital stay were analysed for possible drug interaction via the electronic database MEDSCAPE database. The type and severity of the identified interacting pairs was documented as per the database. Also, the risk factors associated with the potential DDIs were studied.

Statistical analysis

Descriptive statistics, t were used to analyse the results. Descriptive statistics were used for summarizing the demographic parameters and potential DDIs.

RESULTS

A total of 150 ICU patients who fulfilled the inclusion and exclusion criteria were enrolled into the study. Among them, prescriptions of 150 patients were found to have at least one potential interacting drug combination. The overall incidence rate was found to be 98%.

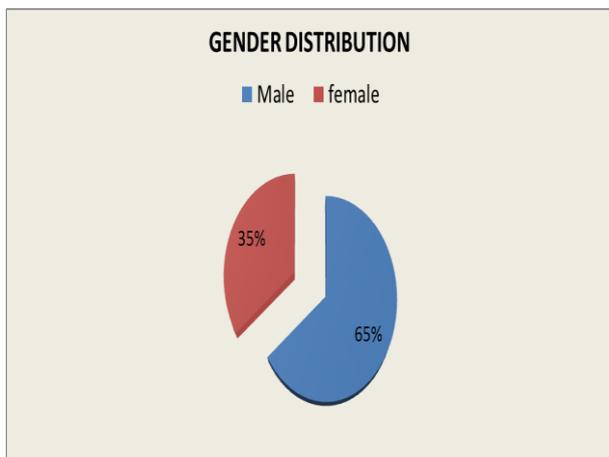


Figure 1: Shows the genderwise distribution of drug reactions males are affected more than females.

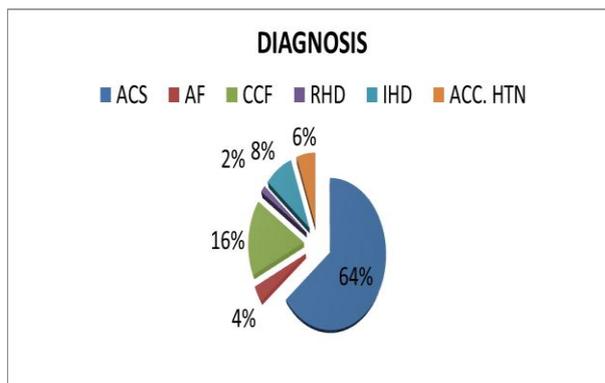


Figure 2: Shows the commonly seen conditions in ICU, ACS found to be the most commonly seen disease Whereas RHD is the least.

Table 1: Number of drugs per prescription.

	Mean	Standard deviation
Total number of drugs per prescription	8.3651	2.4152
Total number of DDIs per prescription	6.0109	3.1099

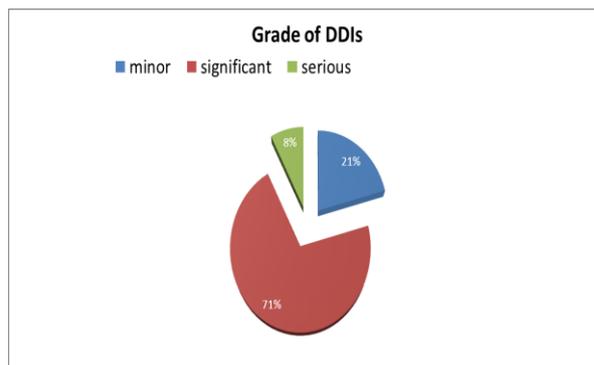


Figure-3.

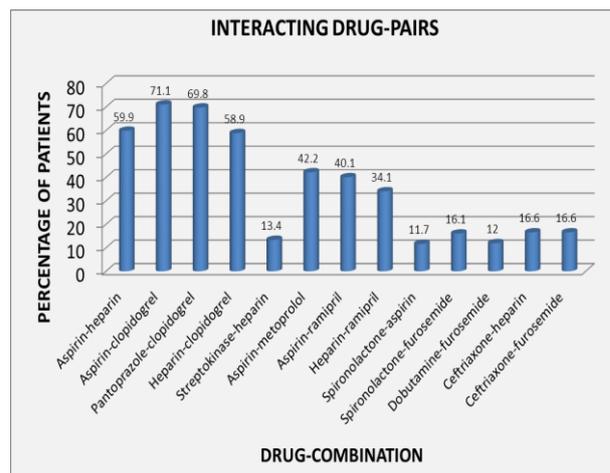


Figure-4.

Among all the interaction pairs the most commonly observed interaction pair was Aspirin – Clopidogrel (71.1%) and least interaction seen with the pair is Spirolactone-Aspirin (11.7%).

DISCUSSION

In drug-drug interactions (DDIs) one of the factors that can alter the response to drugs is the concurrent administration of other drugs.^[6] There are several mechanisms by which the drugs may interact, but most can be categorized as Pharmacokinetic interaction occurs when either of the concurrently administered drugs have potential to alter other's pattern of absorption, distribution, metabolism and excretion. pharmacodynamic (additive, synergistic or antagonistic effects) or combined interactions.^[7]

Drug-drug interactions may be beneficial or harmful. Harmful drug-drug interactions are important as they cause 10 - 20% of the adverse drug reactions requires hospitalisation and they can be avoided.^[10] The potential benefits of drug combinations should be weighed against the seriousness of the DDI, taking into account the availability of alternatives. If the benefit of treatment is of such importance that it outweighs the potential risks, and no safer alternatives are apparent, then the risks of a potential DDI may be tolerated and treatment continued.^[3]

The present study showed the pattern of pDDIs among patients admitted to Sri Chamarajendra hospital attached to HIMS Hassan. The incidence rate of pDDIs was 98% whereas similar studies showed 30.67%,^[11] 21.3%^[7] and 91.6%^[4] the higher incidence of interactions may be due to irrational use of two or more drugs.

The present study showed a higher incidence of pDDIs in males compared to females. whereas other studies showed higher incidence in females,^[6] but differs from a study done by Murtaza *et al.*^[4] which showed no significant association between pDDIs and gender. Also, the incidence rate of pDDIs showed an increasing trend with age and this could be because the mean number of drugs per prescription was higher in the elderly patients due to coexisting co-morbidities.^[12] Variation is may be due to incidence of cardiovascular disease common in males than that of the females.

In the present study, a higher number of observed pDDIs were due to pharmacodynamic mechanisms (82%) compared to pharmacokinetic type of interactions (18%). These findings differ from those reported by Vonbach *et al.*, Aparasu *et al.* and Sharma *et al.*^[7,13,14] This difference may be due to differing patterns of prescription in various settings where the studies were conducted.

On analysis the severity of the interactions, majority of the identified pDDIs were of significant grade (71%) as per the MEDSCAPE database. Only (8%) interactions were found to be of severe grade. These results correlate well with the observations made in other studies where different electronic software was used to identify the pDDIs and majority of the identified interactions were of moderate severity.^[4,7]

Our study showed Aspirin/clopidogrel (71.1%) and pantoprazole/clopidogrel (69.8%) were the most common interacting pairs. Drugs most commonly involved were Aspirin, Clopidogrel, Heparin, Pantoprazole and Ramipril. These findings are similar to study done by Patel *et al.*^[11] and Smithburger *et al.*^[15] but differ from observations done by Sharma *et al.*^[7] where atorvastatin and enalapril were the most common drugs involved in DDIs. Our study includes most of the cardiovascular disorders so Aspirin is most commonly used in most of the cases both for treatment and prophylaxis.

CONCLUSION

The high incidence of potential DDIs among cardiac inpatients in our study highlights the need to take appropriate measures to keep a check on some of the potentially hazardous consequences. Some of the potential consequences of the observed pDDIs were hemorrhage, alteration in serum potassium levels, hypoglycaemia, digoxin toxicity, nephrotoxicity and reduced efficacy of certain anti-hypertensive agents. Age, female gender, duration of hospital stay, stay in ICU for a minimum duration of 24 hours, number of medicines prescribed and presence of diabetes mellitus were the risk factors identified in this study. One of the ways to minimize the consequences of DDIs would be to use the DDI database freely available online, both by clinicians as well as pharmacists. Also, proper therapeutic planning as well as routine monitoring of serum electrolytes, blood glucose and coagulation profile in cardiac in-patients is most important. At the same time confirmation of pDDIs clinically as well as by pharmacokinetic studies especially for significant and severe DDIs seems essential.

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