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Study of Prevalence of Potential Drug Interactions in Medicine Wards at A Tertiary Hospital.

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ABSTRACT

A drug-drug interaction is said to occur when the effect of a drug is altered by concurrent administration of another drug. There is a need to know and understand the commonly occurring preventable interactions. This cross sectional, observational study was carried out for the surveillance of the same. One prescription per patient was collected on their 3rd day of hospitalization and analyzed for the likelihood of potential drug-drug interactions by using online data base-Medscape drug interaction checker and standard references. Parameters calculated were, average number of drugs per prescription, percentage of prescriptions having at least 1 pair of interacting drugs, average number of potentially interacting drug pairs per prescription, and classification of interactions based on mechanism and severity. An average of 6 medications was prescribed per patient. Potential drug--drug interactions were encountered in majority of prescriptions, 90% appeared to be non intentional. 53% were minor in severity, rest were moderate or severe; requiring monitoring, alteration of drug therapy, or intervention. Such studies put forth the common drug interactions which we come across. Most are preventable; their knowledge can help practitioners prevent the concomitant use of dangerous medication combinations.

Keywords: potential drug-drug interactions, pharmacokinetic, pharmacodynamic, minor moderate or severe interactions

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INTRODUCTION

A drug interaction may be said to be occurring when 'the pharmacological or clinical response to the administration of a drug with another agent is different from that anticipated from the known effects of the two agents given alone.' In other words, they occur when the effects of one drug are changed by the presence of another drug, food, drink, or some environmental chemical agent. Drug-drug interaction refers to modification of response to one drug by another when they are administered simultaneously or in quick succession. Drug interactions represent major problems in day to day practice. The incidence of adverse reactions increases exponentially as the number of drugs co-prescribed rises, and this is in part due to interactions. Critically ill, chronically ill, and elderly patients are particularly at risk of clinically manifest drug interactions [1].

The incidence of clinically significant drug interactions is difficult to assess. Studies in this area are hampered by the lack of an agreed definition for drug-drug interactions (DDIs) and the lack of an agreed standard list of DDIs against which adverse events can be correlated. The list of adverse DDIs is already quite long and constantly growing. It is practically impossible for anyone to know and remember all possible drug interactions. Fortunately, the clinically important and common drug interactions that may be encountered in routine practice are relatively few. Exhaustive compilations and documentation are available in specialized books, monographs, review articles and computer database on the subject, but these also need constant updating [2].

DDIs may arise by multiple mechanisms

Pharmacokinetic Mechanisms

The gastrointestinal absorption of drugs may be affected by concurrent use of other agents that (1) have a large surface area upon which the drug can be adsorbed, (2) bind or chelate, (3) alter gastric pH, (4) alter gastrointestinal motility, or (5) affect transport proteins such as P-glycoprotein and organic anion transporters.

The mechanisms by which drug interactions alter drug distribution include (1) competition for plasma protein binding, (2) displacement from tissue binding sites, and (3) alterations in local tissue barriers, for example, P-glycoprotein inhibition in the blood-brain barrier.

The metabolism of drugs can be stimulated or inhibited by concurrent therapy, and the importance of the effect varies from negligible to dramatic. Induction of cytochrome P450 isozymes in the liver and small intestine can be caused by drugs, enzyme inducers can also increase the activity of phase II metabolism such as glucuronidation.

The renal excretion of active drug can also be affected by concurrent drug therapy. P-glycoprotein, organic anion and cation transporters are involved in active tubular secretion of some drugs, and inhibition of these transporters can inhibit renal elimination with attendant increase in serum drug concentrations.

Pharmacodynamic Mechanisms

When drugs with similar pharmacologic effects are administered concurrently, an additive or synergistic response is usually seen. Conversely, drugs with opposing pharmacologic effects may reduce the response to one or both drugs. Pharmacodynamic drug interactions are relatively common in clinical practice, but adverse effects can usually be minimized if one understands the pharmacology of the drugs involved. In this way, the interactions can be anticipated and appropriate countermeasures taken.

Combined Toxicity

The combined use of two or more drugs, each of which has toxic effects on the same organ, can greatly increase the likelihood of organ damage.

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The risk and severity of drug interactions varies under the influence of factors such as number of medications received, duration of treatment, patients' age, the number of prescribing physicians and stage of disorder [3]. It is said that Adverse drug events per se account for 19% of all adverse events and 5–26% out of these are generated by DDI. They pose a significant risk to the patient's health outcomes and a considerable economic burden on the health care system [4].

So, it is prudent to monitor the DDIs in patients who are on polypharmacy and to collect the data regarding the various commonly occurring drug interactions. With this background, the aim of this study was to monitor the potential drug -drug interactions in the patients of the medicine ward at a tertiary care hospital.

MATERIALS AND METHODS

This cross sectional, observational study was performed at the medicine wards of a tertiary care teaching hospital. The data was collected over a period of 1 month. Patients of either sex admitted to the wards were included if they were aged 12 years or more and receiving drugs for a minimum period of three days. The investigator visited the wards daily and collected data from patients' case records. Only one prescription was included for each patient on his/her 3rd day of hospitalization in the ward. Information collected included demography of the patient, the detailed prescription.

The prescriptions were analyzed for likelihood of potential drug interactions by using the online data base-Medscape Drug Interaction Checker [5] and cross checked from Pubmed and Pharmacology textbooks.

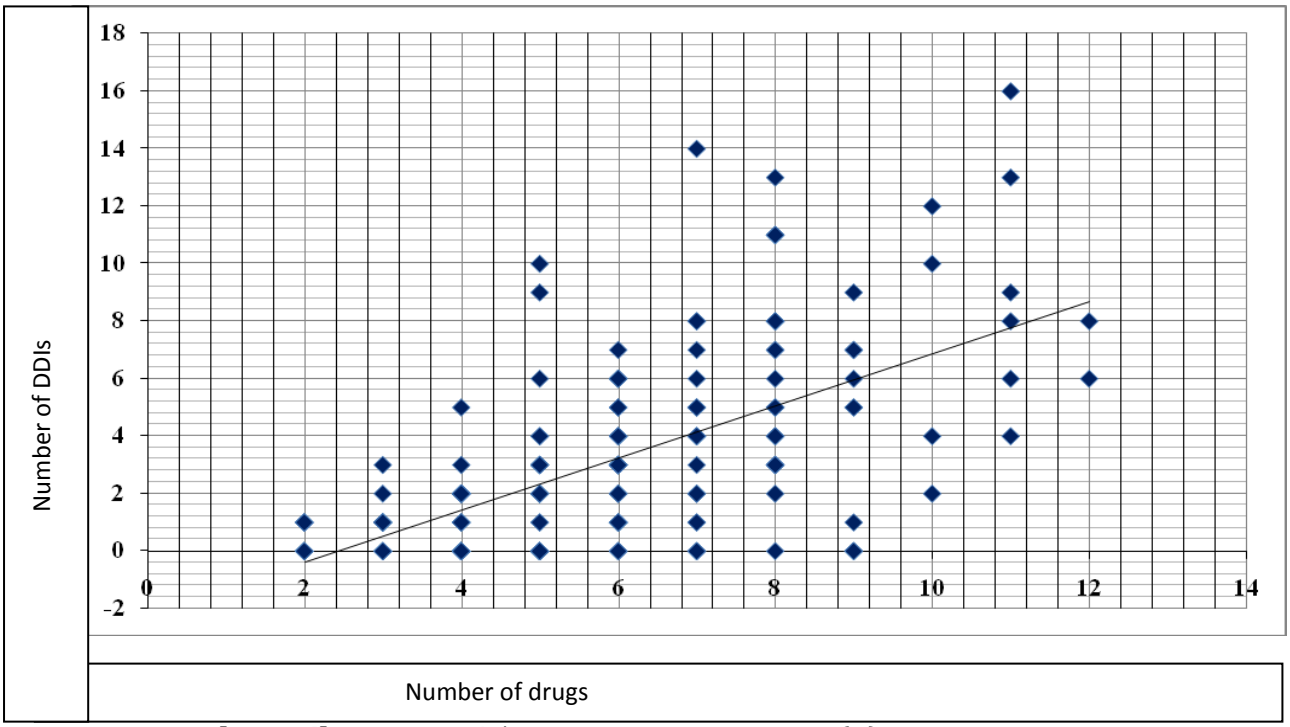
The data was analyzed for the following descriptive parameters

- The average number of drugs per prescription
- % of prescriptions having probability of at least 1 pair of interacting drugs
- Average number of such potentially interacting drug pairs per prescription
- Classification of the potential drug interactions based on intention, mechanism and severity

RESULTS

A total of 1189 drugs were prescribed in 200 prescriptions, resulting in an average of 5.9 drugs per prescription. As the number of prescribed drugs per prescription increased, so did the number of potential DDIs, as is evident from the scatter diagram in Figure 1.

Figure 1: Number of drugs per prescrition vs Interactions



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A total of 638 potential DDIs were noted. The majority were seen in middle aged and elderly people (Table 1).

Table 1: Age distribution of patients along with frequency of potential DDIs

Age group (years)	Number of Patients	Number of DDIs noted
< 20	25	71
21 -30	30	95
31-40	36	77
41-50	41	138
51-60	36	109
61-70	26	137
>70	6	11

Figures 2, 3 and 4 depict classification of the potential DDIs based on Mechanism, Intention and Severity.

Figure 2: Classification of interactions based on mechanism

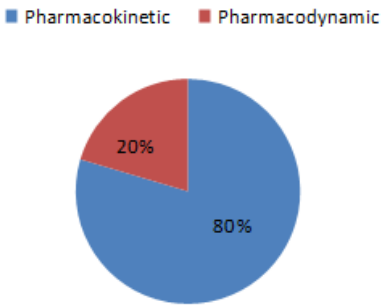

Figure 3: Classification of interactions according to purpose: Intentional or Unintended

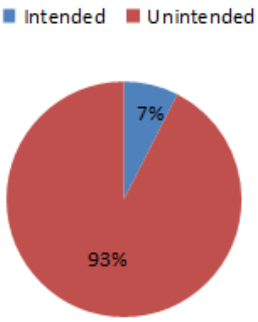

Figure 4: Classification of interactions based on Severity

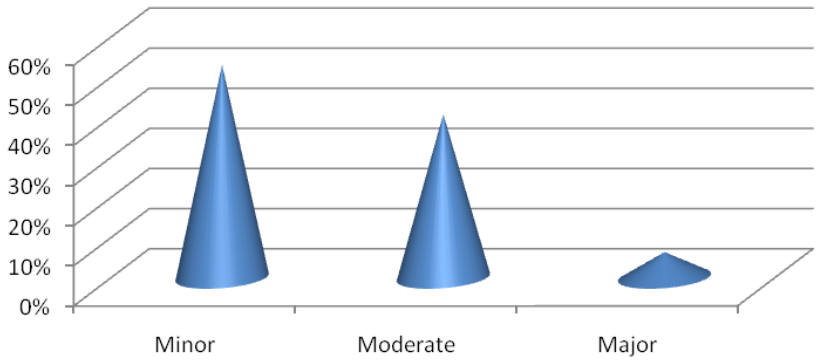

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Table 2: Most common interacting drug pairs

Type of interaction	Most commonly found interacting pair	Number of prescriptions with the interacting pair
MINOR	Ranitidine + Vitamin B12	53
MODERATE	Ranitidine + Ferrous Sulfate	10
MAJOR	Octreotide + Ondansetron	5

79.6% (508/638) were Pharmacokinetic in nature, while 20.4% (130/638) were Pharmacodynamic interactions. The majority were unintended interactions (92.5%) while a few like Aspirin + Clopidogrel, Furosemide + Spironolactone were intentional (7.5%).

The non intentional potential DDIs were further classified according to their severity and their frequency was as follows-

- Minor 53% = 313/590
- Moderate 40.7% = 240/590
- Major 6.3% = 37/590

The most common drug interacting drug pairs are enlisted in Table 2, wherein

Minor

Refers to the effects of the interaction as usually mild, consequences may be bothersome or unnoticeable but should not significantly affect therapeutic outcome.

Moderate

Effects may cause deterioration in a patient's clinical status. Monitoring of ongoing therapy recommended.

Major or Serious

Interaction may be life threatening and requires medical intervention Or change in therapy to prevent severe adverse effect [5].

DISCUSSION

Studies with potential drug-drug interactions have been conducted in the country and world over. The number of DDIs in our study increased with the number of drugs prescribed, as also reported by Rafei, Arab, Ranjbar in their study in ICU at a tertiary hospital in Iran [6].

Teixeira, Crozatti, Santos reported a high prevalence of DDIs in elderly population in Brazil. Similar results were seen with our study [7]. A number of factors could be responsible for this including polypharmacy, medication errors, inappropriate use of medications, and self medication.

78 % of the prescriptions had at least one potential DDI. However, 25 % of these were minor or non significant in nature. In a similar study by Soherwardi et al, the incidence of potential DDIs was 66 % in a tertiary hospital in South India, although one fourth of them were major [8].

Only 7.5 % of the interactions were beneficial in our study, whereas the proportion was 33.1 % as reported by Rafei et al [6].

Patel, Rana, Suthar evaluated prescriptions for potential DDIs in Ahmedabad and found serious, moderate and minor DDIs at their hospital to be 3.6 %, 73.37 % and 22.94 % respectively, while at our setup it was 6.3 %, 40.7 % and 53 %.[9].

Most common Minor interaction was found to be between Ranitidine and Vitamin b12. Ranitidine decreases the level of Cynacobalamin by inhibiting GI absorption. It is not clinically important in short term use, but long term use may contribute to the occurrence of Iron/Cobalamin deficiency anaemia.

Most common moderate interaction was after the co administration Ranitidine and Ferrous Sulfate. Ranitidine decreases the level of Ferrous Sulfate by increasing gastric pH. The two should be administered with a gap of 2 hrs.

Most common serious interaction was between Octreotide and Ondansetron. Both prolong QT interval. ECG monitoring recommended especially in case of electrolyte abnormalities, congestive heart failure, bradyarrythmias.

The majority of potential DDIs were Pharmacokinetic in mechanism, while in a study by Kulkarni et al in South India, 42 % were Pharmacokinetic, 24 % Pharmacodynamic and the rest unknown [10]. Prescribers need to be sensitized about the possible occurrence of serious drug interactions so as to avoid using drug combinations leading to them. Knowledge about the mechanism of interaction helps the practitioner to administer the drugs in such a way that therapeutic benefits of the drugs are maximized and harmful interaction between them avoided.

CONCLUSION

The study put forth the commonly occurring potential DDIs at the Medicine wards at our tertiary hospital. Clinically encountered DDIs were not taken in account, which stands as a major limitation in the study. Although the clinically encountered ones may be less in number and severity, such a study does sound a warning bell about their occurrence. The study focused only on one department, and prescriptions were collected over a short duration. Drug disease interaction is another area of research which was not included. The results highlight the importance of rational prescribing, improving awareness about the possibility of drug interactions, use of online databases to check them, and taking steps to minimize them. Spontaneous reporting of adverse drug reactions by physicians to the respective Pharmacovigilance centre will also go a long way in increasing our knowledge about this important health issue. Inclusion of lecture series, case presentation sessions related to drug interactions and adverse drugs reactions and training programs for post graduate students may help in rational prescribing and averting potentially harmful drug interactions.

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