Research Article

A Study of the Possible Drug-Drug Interactions in Medicine Unit of A Tertiary Care Hospital

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ABSTRACT

An interaction is said to occur when the effects of one drug are altered by the co-administration of another drug, herbal medicine, food, drink or other environmental chemical agents. This study was designed to analyze the possible drug-drug interactions in the medicine department of a tertiary care hospital. A prospective study was conducted on inpatients admitted to the medicine department of a tertiary care hospital for a period of 6 months. The patient demographics, diagnosis and drugs prescribed were recorded and presence of possible drug-drug interactions were detected using standard databases. Out of 60 cases collected, 36(60%) and 24(40%) were men and women respectively, where interactions were seen in 47% of male patients and 50% of female patients. A total of 682 drugs were prescribed at an average of 11 drugs per prescription. A total of 665 possible interactions were reported. Major interactions were 36 (5%) and moderate interactions were 550 (83%). Aspirin had the highest number of interactions with involvement in 65 types of moderate and 6 types major interactions. As per the study, among the top 5 drug combinations involved in drug-drug interactions, Aspirin+ Insulin combination was found to have the highest prevalence (36%). The study observed increased number of possible interactions with increase in number of drugs/prescriptions. This study reported a total of 665 interactions. Aspirin was involved in most of the drug interactions. Aspirin and Enoxaparin was the most frequent interacting drugs.

Keywords: Drug interactions, Aspirin, Insulin, Enoxaparin, prescription.

INTRODUCTION

Medication errors are responsible for 16 - 20% of all adverse events in any hospital setting. A drug-drug interaction (DDI) is one type of medication error and is a physiological response to a combination of drugs that results in an outcome, which differs from the responses to the agents when administered individually. Some interactions are deliberate because of their synergistic effect. Some drug interactions are undesirable. Drug-drug interactions account for nearly 19% of drug-related adverse effects. Most of the interactions do not cause any harm to the patient, but some have the potential to cause significant morbidity. Majority of the drug-drug interactions can be identified and prevented before they can cause any harm to the patient.[1]

Risk factors for Drug Interactions:

a) Drugs with a narrow therapeutic index: Where a small margin exists between therapeutic and toxic drug levels and above these accepted levels these drugs may show many unwanted effects. For the other drugs with a wide therapeutic index e.g. penicillin's and many benzodiazepines, a 20-50% change in concentration may not show any adverse drug reaction.

b) High-risk patients: Drug interaction has a very good correlation with polypharmacy. Polypharmacy in the elderly is the major reason for drug interaction. According to literature, patients taking 2-5 drugs daily suffer potential drug interaction with the incidence being 19%. This incidence rises to 80% for those taking 6 or more drugs. Ability to metabolise drug is influenced by renal or hepatic impairment, which is very common in elderly. Patients with severe underlying disease may be less tolerant of changes in plasma concentration of their therapy. The current clinical condition may also influence drug interactions as can the patients pre-existing clinical status.

c) Genetic characteristics may affect some drug interactions e.g. grapefruit juice and terfenadine resulting in an increased risk of cardiotoxicity. In the case of Terfenadine, a small number of population is poor metaboliser of Terfenadine. This risk factor may also explain the interactions involved with Warfarin and tricyclic antidepressants. [1]

There are several classifications of drug-drug interactions and one of the most important is the one according to severity: drug-drug interactions could be major, moderate and minor.

1) Major: The effects are potentially life-threatening or capable of causing permanent damage.

2) Moderate: The effects may cause deterioration in patients' clinical status and additional treatment or extension of hospital stay.

3) Minor: The effects are usually mild. [2]

Pharmacists have a central role in ensuring medication safety across the continuum of care. This study was conducted in the medicine department of a tertiary care hospital to identify the severity of interactions, risk factors for interactions and to know the most common drugs involved in drug interactions.

STUDY DESIGN

This study is a prospective, observational study, conducted at Sagar Hospitals, Bengaluru, a 150 bedded multidisciplinary tertiary care hospital, over a period of 6 months.

Study Population

The study was conducted in the medicine unit of a tertiary care hospital. The data was collected from the patients admitted as inpatients. Most of the patients belonged to the middle and upper strata of the society.

Study Protocol

Study protocol was prepared by conducting extensive literature search. It contained information on need for the study, objectives, review of literature, methodology and was submitted to Dayanand Sagar College of Pharmacy Institutional Human Ethical Clearance Committee for approval.

The study was approved by institutional ethics committee and issued ethical clearance certificate for the same.(Reference No. DSCP/P-D/IHEC/2018-19/015)

The patients were enrolled into the study as per the inclusion and exclusion criteria stated in the study protocol.

Inclusion Criteria:

- All the patients of either sex who are diagnosed in inpatient department
- Patients being treated with various medications

Exclusion Criteria:

- Pregnant women
- Critically ill patients

Source of Data:

- Patient case sheet
- Patient Interview
- Laboratory data reports

Study Procedure:

The prescriptions were chosen based on inclusion and exclusion criteria. After obtaining the consent, details of the patient were followed till discharge. During the study the inpatient case record was reviewed which included patient demographics, specific information such as name of medications, their dosage schedule, date of discontinuation, concomitant medications, lab investigations, diagnostic procedures and treatment details. The information collected was documented in the patient profile form. The drug interactions were assessed using the Micomedex database and websites like www.drugs.com and www.medscape.com.

RESULTS

A total of 60 patients were enrolled in the study.

Demographic characteristics of patients:

Gender

Table 1: Gender wise distribution of patients

Gender	No. of patients (Percentage)
Male (%)	36(60%)
Female (%)	24(40%)

Among 60 patients enrolled in study, majority of the population included male patients.

Age

Among 60 patients from the study population, average age of the male population was found to be 52 years and that of the female population was found to be 43 years.

Table 2: Average age of Study Subjects

Gender	Male	Female
Average age in years	52	43

Average number of drugs per prescription

Out of all the 60 prescriptions studied, a total of 682 drugs were prescribed and the average number of drugs per prescription was 11.

Table 3: Average Number of Drugs per prescription

1.	**Total No. of Drugs in 60 prescriptions**	682
2.	**Average Number of Drugs per prescription**	11

Number of drugs per prescription

Maximum number of cases (23) comprised drugs in the range of 7-12.

Table 4: Classification of Drug Interaction Cases based on number of drugs per prescription

S.No.	No. of drugs/Prescription	No. of Cases
1.	1-6	13
2.	7-12	23
3	13-18	18
4.	19-24	5
5.	25-30	1

Classification of drug interactions

As per this study, it was found that majority of the interactions (92%) were moderate in nature, and 8% of the interactions were major in nature.

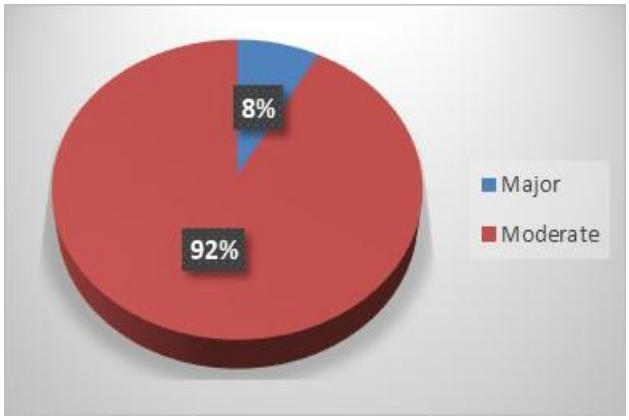

Figure 1: Classification of Drug Interactions Based on the Severity

Average number of interactions

Among the 60 cases studied, it was found that the highest number of interactions were from cases with the highest number of drugs (25-30).

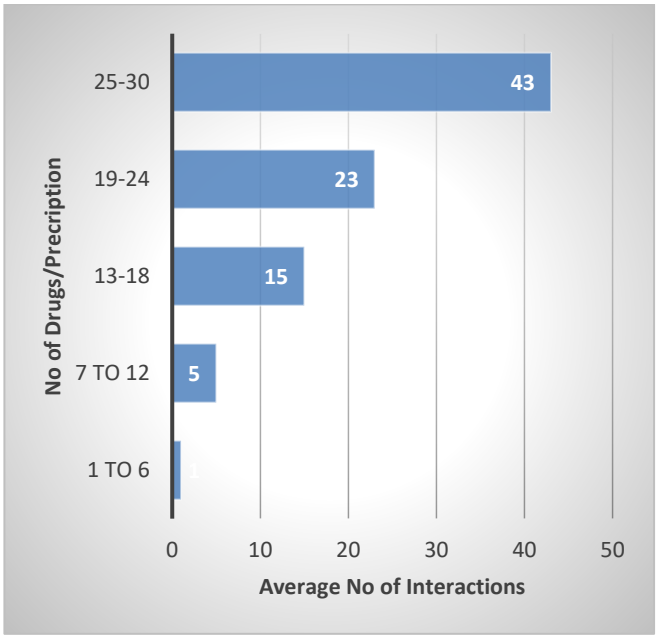

Figure 2: Average No of Interactions based on number of drugs prescribed

Drugs involved in interactions

As per the study, among the top five drugs involved in potential drug interactions, aspirin was involved in the highest number of drug interactions (Moderate-65, Major-6) and furosemide had the lowest among the lot (Moderate-21, Major-0).

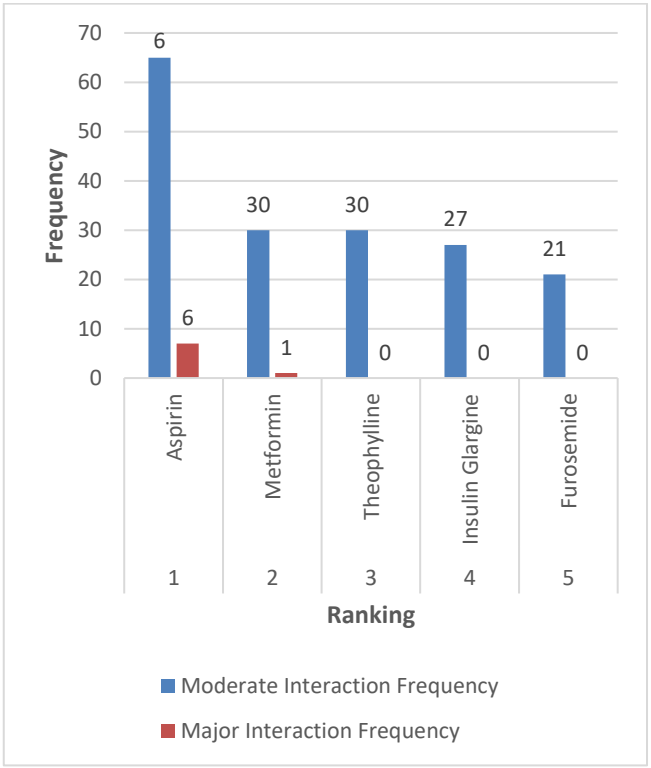

Figure 3: Top Five Drugs Involved in Drug Interactions

Top drug combinations

As per the study, among the top 4 drug combinations involved in drug-drug interactions, Aspirin+Insulin combination was found to have the highest number of drug-drug Interaction with 36% prevalence and Levothyroxine+Metformin occupied the 4th place with 13% prevalence.

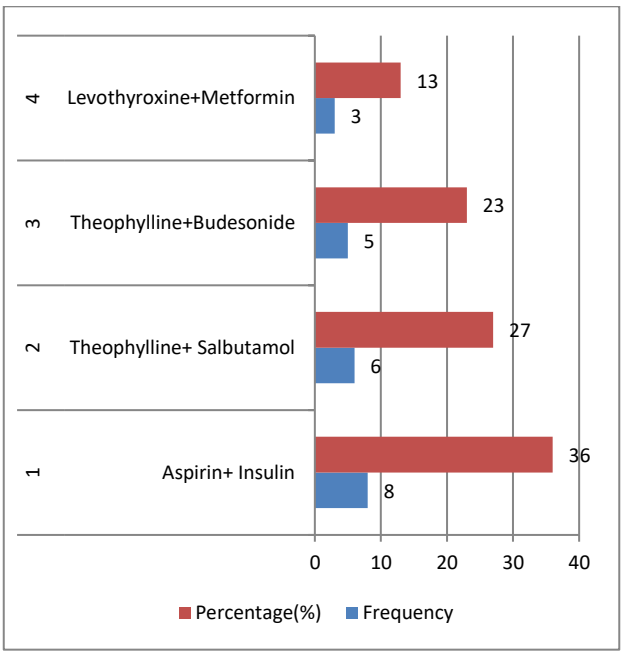

Figure 4: Top 4 drug combinations involved in drug-drug interactions

DISCUSSION

In this study, an attempt has been made to describe the various potential drug-drug interactions and their considerable impact in the healthcare environment.

A total of 60 patients were enrolled in the study, number of male patients were more than number of female patients as illustrated in Table No. 1. In a similar study conducted by Biradar S.M. et al, it was found that out of 104 patients, males were 54% and the number of female patients was 46% and the study by Bethi Y et.al, also reported a higher number of male patients compared to female patients. [3,4]

The average age of male subjects was found to be 52 years and that of female patients was found to be 43 years indicating that females were admitted to the hospital at a younger age compared to males.

As per this study, out of all the 60 prescriptions studied, a total of 682 drugs were prescribed and the average number of drugs per prescription was 11. The average number of drugs prescribed is much higher than the similar study by Subramanian A, et al., where it was 5.[5] The higher number of drugs per prescription in this study can be a result of the severity of the illness in study group.

It is recommended that the average number of drugs per prescription should be as low as possible failing which it can lead to polypharmacy. The term polypharmacy is commonly applied to situations where patients take five or more medications. Some of the consequences of polypharmacy are increased risk of medication errors, drug-drug interactions, sub-optimal patient adherence, reduced quality of life. From Table No.3, we can observe that as the number of drugs/prescription increase, the number of interactions is also increasing. Hence, we can come to the sequitur that polypharmacy can be observed in this study which is the absolute indicator for increased risk of drug interactions, adverse effects, development of bacterial resistance and increased hospital cost.

In this study majority of interactions were moderate in nature (92%). Moderate interactions can be defined as those which may result in exacerbation of the patient's condition or result in alteration of therapy which is in concordance with a study conducted in a university hospital in Iran where moderate interactions were 74% [6]and one more study conducted in the South Indian teaching hospital which reported 70% of interactions as moderate.[7]

Among the 60 cases studied, it was found that the highest number of interactions were from cases with the highest number of drugs (25-30). This observation proves the fact that polypharmacy leads to an increased number of the drug interactions leading to higher probability of adverse drug reactions and non-adherence. This is similar to a study by Avery et.al, according to which error rate increased (in other words medication errors like possible drug-drug interactions increased) with the number of drugs prescribed.[8] It is also similar to a study by Dubova et.al which states that, "high frequency of prescription of drugs with potential drug interactions is common in primary care level; the easiest way to reduce the frequency of them is to decrease the number of medicines prescribed." which further supports our findings.[9]

In Figure No 3. as per the study, among the top five drugs involved in potential drug interactions, Aspirin was involved in the highest number of interactions (Moderate-65, Major- 6). Most of the interactions involving Aspirin had a mechanism of effect resulting in an increased risk of bleeding. Most of the interactions involving Metformin had an increased risk of decreased efficacy of Metformin which led to interference in blood glucose control. Most of the interaction involving Theophylline had increased risk of cardiovascular effects like palpitations, tachycardia etc. Most of the interactions involving Furosemide had a mechanism of effect resulting in an increased risk of diuresis and loss of minerals like potassium, magnesium and sodium. Most of the interactions involving Insulin had an increased bioavailability of Insulin which results in a potentiating hypoglycemic effect. These results were in solidarity with the study by Patel et al.[10]

In Fig.No.4, as per the study, among the top 4 drug combinations involved in drug-drug interactions, Aspirin+Insulin combination was found to have the highest number of interactions with 36% prevalence and a frequency of 8. A study by Mohammed Ismail et.al, also observed this interaction as one of the frequent interactions.[11] The interaction between Aspirin +Insulin leads to an increased bioavailability of Insulin which results in a potentiating hypoglycemic effect.

The next combination in the list, Theophylline+Salbutamol may increase cardiovascular side effects such as heart palpitations, increased heart and pulse rates, and blood pressure elevations. Combining these medications may also increase the risk of developing hypokalemia. The incidence of Theophylline+Budesonide interaction was 23%. The concomitant use of this combination may theoretically increase the risk of hypokalemia due to additive potassium lowering effects. Additionally, theophylline serum concentrations may be altered. The mechanism is unknown and data have been limited and conflicting; increased, decreased, and unchanged theophylline levels have been reported. This result is similar to the study result of Ahmad et.al,[12] where Theophylline +Budesonide had a prevalence rate of 13.66%. The interaction between Levothyroxine +Metformin had 13% prevalence. The interaction between Levothyroxine and Metformin caused a decreased efficacy of Metformin thereby interfering in blood glucose control. Some studies also suggest reduced efficacy of Levothyroxine as seen in a study by Carlo Cappelli et.al.[13]

CONCLUSION

This was a study conducted in the medicine department of a tertiary care hospital. The average number of drugs/prescriptions was high clearly indicating the presence of polypharmacy. As expected, the presence of polypharmacy resulted in a proportional increase in the number of possible interactions between the drugs. The drug Aspirin used as an antiplatelet agent was most commonly involved drug followed by Metformin, Theophylline and Insulin glargine. The most common possible drug interaction were interactions between Aspirin+Insulin; Theophylline+Budesonide; Levothyroxine +Metformin & Theophylline+Salbutamol. A Clinical Pharmacist can play an important role in the identification, prevention, reporting and management of drug interactions by effective prescription monitoring & communication to other healthcare professionals.

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