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A PROSPECTIVE OBSERVATIONAL STUDY OF POSSIBLE SIGNIFICANT DRUG-DRUG INTERACTIONS IN SURGICAL GASTROENTEROLOGY DEPARTMENT IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Drug-drug interaction may lead to serious health problems hence detecting and avoiding the concomitant use of interacting agents are necessary. **Aim:** Identification and reporting of possible significant drug interactions in surgical gastroenterology department in a tertiary care hospital. **Objective:** The main objective of the study includes preventing and monitoring drug interactions, identifying and minimizing medication related problems, improving patient safety, providing better therapy, improving the Patient health related outcomes **Material and methods:** A Prospective observational study conducted for a period of two months. DDIs were analyzed using Computerized database system Lexi-comp. **Results:** Total 160drug – drug interaction were screened in which 33(20.6%) were major interactions, 38(23.7%) were moderate interactions and 89 (55.6%) were minor interactions. Out of total interactions, 91.25% were pharmacodynamics drug-drug interaction and 8.75%were pharmacokinetic drug-drug interaction. Patients with less than or equal to 5 drugs prescribed per day have 28% interaction and patients with more than 5 drugs prescribed per day have 71% possible drug drug interaction. **Conclusion:** Clinical pharmacist have significant role in identifying and controlling possible major interactions.

KEYWORDS: Drug-drug interactions, Surgical gastroenterology, Patient safety, Clinical Pharmacist.

INTRODUCTION

Drug–drug interactions (DDIs) has received a great deal of recent attention from the regulatory, scientific, and health care communities worldwide. As new drugs are introduced every year, more interactions between medications has been increasingly reported.[4]

Drug-drug interaction is defined as the pharmacologic or clinical response to the administration of a drug combination that is different from the anticipated effects of the two drugs when given alone.[1] Drug-drug interactions are important as they require hospitalization due to adverse drug reactions, decreased therapeutic benefit, and are an avoidable cause of patient harm. It may occur due to either toxicity or therapeutic failure. Elderly patients are more vulnerable with a strong relationship between increasing age, polypharmacy and the frequency of potential drug–drug interactions.[1] Concomitant use of more than five drugs is defined as polypharmacy.[10] Polypharmacy often results in heightened risk of drug related problems and also results in greater healthcare costs, increased risk of adverse drug events, drug–drug interactions (DDIs), and medication nonadherence.[11]

The more drugs a patient takes the greater the likelihood that an adverse reaction will occur. One hospital study found that the rate was 7% in those taking 6 to 10 drugs but 40% in those taking 16 to 20drugs, which represents a disproportiate increase because of the interacting drugs.[9] Drug– drug interaction considered as a risk factor for patient safety, Therefore it has become a general concern and concept in terms of appropriate therapy.[4]

Drug interactions fall into three broad categories

- **Drug-drug i**nteractions occur when two or more drugs react with each other.
- **Drug-food**/beverage interactions result from drugs reacting with foods or beverages
- **Drug-condition** interactions may occur when an existing medical condition makes certain drugs potentially harmful.[2]

Drug interactions that cause important changes in the action of a drug are of the greatest concern where as those which are rare, or minor are unimportant. Drug interactions are complex and unpredictable. A known interaction may not occur in every individual as it is likely to occur based on the following factors:

- Genes
- Physiology

- Age
- Lifestyle (Diet, Exercise)
- Underlying diseases
- Drug doses
- Combined therapy duration and time of administration of two drug.[8]
- Drug interactions involve:
- Pharmacodynamics
- Pharmacokinetics

In pharmacodynamics interactions, one drug alters the sensitivity or responsiveness of tissues to another drug by having the same (agonistic) or a blocking (antagonistic) effect. These effects usually occur at the receptor level but may occur intracellularly. In pharmacokinetic interactions, a drug usually alters absorption, distribution, protein binding, metabolism, or excretion of another drug. Thus, the amount and persistence of available drug at receptor sites change.[7]

Important drug interactions occur frequently and they increase the cost of health care. Moreover, many drugs have been withdrawn from market because of their potential to interact with other drugs and cause serious health care problems.[6]

More than 100,000 types of potential drug interactions have been documented, but most do not actually lead to adverse effects. The actual frequency of drug-drug interactions is unknown. One survey of two large health plans using prescription drug claims data estimated the risk of potential drug interactions to be 6.2% to 6.7% per year. The risk of dying from a drug-related incident now exceeds the risk of dying in a traffic accident. In 2008 (the most recent data available), 36,500 drug related deaths were reported. This statistic is a wide net and includes intentional overdose and illicit drug use, as well as adverse drug reactions, drug interactions, and other drug mishaps. In 2010, 3.7 billion prescriptions were filled, averaging about 12 prescriptions per person in the United States. The risk of ADR and drug interactions increases with the number of drugs a patient is taking.[3]

Not all drug interactions are bad. Some drug interactions are used therapeutically. For example:

Reversing agents, such as naloxone, are given after surgery to stop the effects of narcotics. Advanced age is a condition that increases drug interaction risk.[3]

The pharmacist, along with the prescriber are responsible to ensure the patient awareness related to the risk of unexpected effects that may occur due to drug interactions. The unexpected symptoms experienced by patients can also be related to possible adverse effects of drug therapy by a skilled clinical Pharmacist. The practice in clinical pharmacy ensures that drug interactions are minimized by avoiding drugs with potential side effects in susceptible patients. Thus, pharmacist has a major role to play in relation to prevention, detection, and reporting drug interactions.[4]

The study was conducted in department of Surgical Gastroenterology due to potential for drug interaction secondary to the magnitude and type of surgeries. Prokinetics like domperidone and levosulpiride are routinely used to hasten onset of gastrointestinal function following major gastrointestinal surgeries. This is also a part of Fast Track Surgery protocol which enables enhanced recovery and early discharge of patients with its attendant benefits[5]. The most common complication after any abdominal surgery is pulmonary in nature. To prevent this bronchodilator nebulisations are routinely used after abdominal surgical procedures. Antibiotics are used according to culture and sensitivity. Beta lactamase resistant antibiotics frequently need to be used due to prevailing in house sensitivity.

MATERIALS AND METHODS

Study Design

A Prospective Observational study by a Clinical Pharmacist.

Study Period

This study was conducted for a period of two months from April 2018 to May2018.

Study Site

The study was conducted in Surgical Gastroenterology Department at Believers Church Medical College Hospital, Thiruvalla, Kerala.

Sample Size

32 patients who satisfied inclusion criteria and underwent major surgery (>3hours duration) in Surgical Gastroenterology unit in hospital were included in the study.

Identification and analysis of drug-drug interaction

Computerized database system Lexi-comp version: 2.4.1.

Source of Data

All the patients satisfying the inclusion criteria were selected from Surgical Gastroenterology Department at Believers Church Medical College Hospital. All the required data was collected from patients through Patient representative interview and case sheets and treatment charts.

Inclusion criteria

- Patients aged above 10 years.
- Patients having length of stay more than 5 days.
- The Patients who are willing to participate in the study.

Exclusion criteria

- Patients whose duration of surgery is less than 3 hours.
- Patients with previous history of drug allergy.
- Multidrug therapies involving antimalignancy chemotherapy were excluded from the study.

RESULTS

Out of 32 prescriptions, 46.7% were male patients and 53% were female patients. Based on the profile of medications prescribed, the drug–drug interactions were identified and classified according to Lexi Comp database.

Demographic information (age and gender) was obtained from the clinical records.

Age wise distribution of patient population

In this study 32 patients were included. The age wise distribution describes 1 patient (3.123%)was in age group ranging from 10-20, 2(6.25%) were in age group 20-30,3(9.375%) were in age group30-40,4(12.5%)were in age group 40-50,6(18.75%) were in age group 50-60, above 70 years of age 10(31.25%) patients were present.

Table 1: Age wise distribution of patients.

Age in years	Total number of patients	Percentage (%)
10-20	1	3.125
20-30	2	6.25
30-40	3	9.375
40-50	4	12.5
50-60	6	18.75
60-70	6	18.75
Above 70	10	31.25
Total	32	100

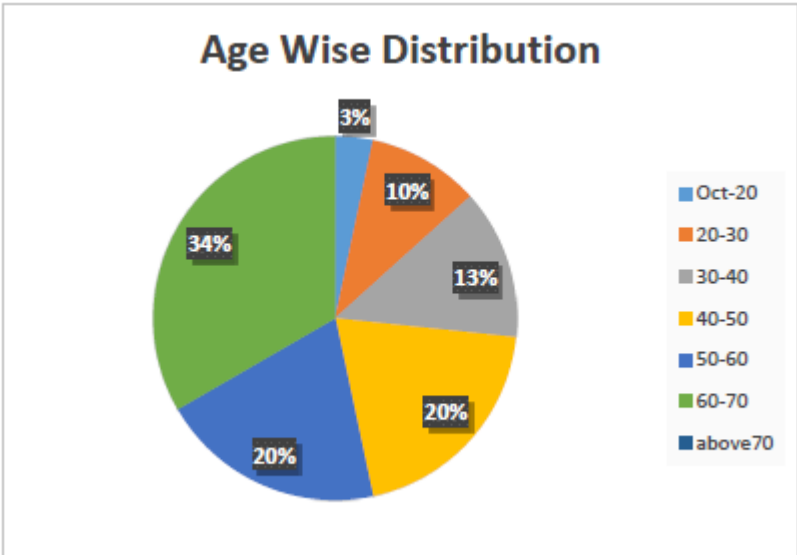

Fig. 1: Age wise distribution of patients.

Gender wise distribution

Total of 32 patients were enrolled in this study out of which 15 patients were male (46.8%) and 17 were female (53.12%).

Table 2: Gendrer wise distribution of patients.

Gender	Total number of patients	Percentage (%)
Male	15	46.8
Female	17	53.12
Total	32	100

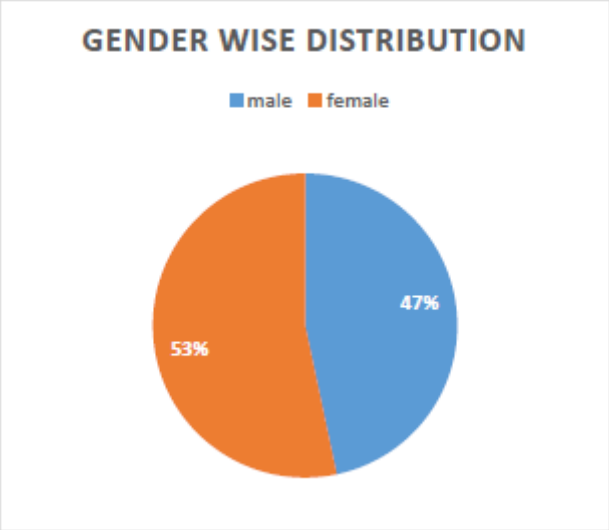

Fig. 2: Gender wise distribution of patients.

Surgical procedure wise distribution.

Table 3: Various surgical procedure done.

Surgical Procedure	Total number of cases
Anterior resection	2
Ileal Pouch-Anal Anastomosis	1
Duodenectomy	1
Excision of Cyst / Tumor	4
Ileostomy Transposition	2
Frey's procedure	1
Laparoscopic Rectopexy	1
Heller's Cardiomyotomy	2
Hepatico Jejunostomy	1
Colectomy / Sigmoidectomy	6
Ventral Hernia Repair	2
Sleeve Gastrectomy	4
Fenestration Cholecystectomy	4
Fundoplication	1
Total cases	**32**

Duration of surgery procedure more than 3 hours were included in the study.

Number of drugs prescribed per day

Table 4: Number of drugs prescribed per patient.

Number of drugs prescribed per day	Number of patients (n=32)	Number of drug interaction (n=160)
≤5	7	45(28.12%)
>5	25	115(71%)

As the number of drugs prescribed per day increases possible drug-drug interaction increases.

Commonly prescribed category of drug

Table 5: Commonly prescribed category of drug in surgical gastroenterology.

Analgesic Proton pump inhibitors			Antibiotics			Antiemetics	
Trama dol	Acetaminophen	Pantoprazole	Piperacillin Tazobactam	Metronida zole	Cefuroxi me	Ondansetron	Domperidone
25	28	30	14	23	5	22	18

Severity of drug interactions

According to severity and rating, drug-drug interactions were classified as:

- **Category X (Major):** Avoid combination altogether
- **Category D (Moderate):** Consider therapy modification
- **Category C (Minor):** Monitor given therapy.

Total 160drug -drug interaction were screened and classified based on severity according to lexi comp database. In which 33(20.6%) were major interactions, 38(23.7%) were moderate interactions and 89 (55.6%) were minor interactions.

Table 6: severity assessment of drug-drug interactions.

Type of severity	Number of drug interactions	Percentage (%)
Major	33	20.6
Moderate	38	23.7
Minor	89	55.6
Total	160	100

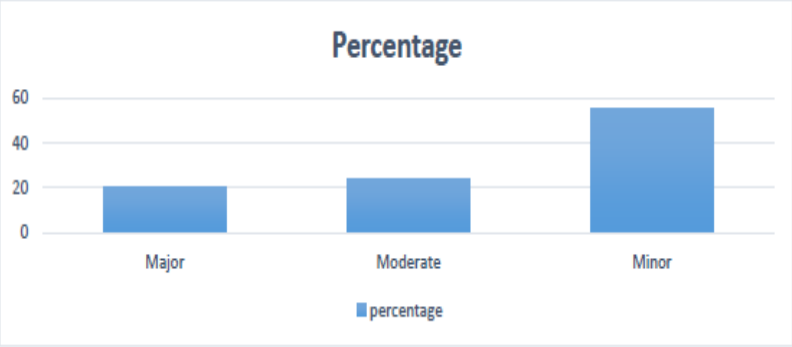

Fig. 3: severity assessment of drug-drug interactions.

Types of drug interactions

Out of 160 interactions, 91.25% were pharmacodynamics drug-drug interaction, 8.75%were pharmacokinetic drug-drug interaction.

Table 7: Types of drug interaction Most common major drug interaction.

Type of interaction	Total number of interactions	Percentage
Pharmacokinetic	14	8.75
Pharmacodynamics	146	91.25
Total	160	100

Table 8: Most common major interactions.

Drug1	Drug2	interactions	Type
Domperidone	Ondansetron	Risk of QTc-Prolongation enhanced.	Pharmacodynamics
Carvedilol	Levosalbutmo1	Beta-Blockers (Nonselective) may diminish the bronchodilatory effect of Beta2-Agonists	Pharmacodynamics
Ipratropium	Levosulpride	Anticholinergic Agents may diminish the therapeutic effect of Levosulpiride.	Pharmacodynamics
Cefuroxime	Pantoprazole	Proton Pump Inhibitors may decrease the absorption of Cefuroxime.	Pharmacokinetic
Olanazapine	Clobazam	Olanazapine may enhance the adverse/toxic effect of Benzodiazepines.	Pharmacodynamics
Ciprofloxacin	Domperidone	Risk of QTc-Prolongation enhanced.	Pharmacodynamics
Domperidone	Escitalopram	Risk of QTc-Prolongation enhanced.	Pharmacodynamics

DISCUSSION

In medical practice, it is common using drug combination which can interact and all DDI detected may not occur in patients, but their identification and reporting is applicable since they may increase the risk of adverse reactions, toxicity or decrease treatment efficacy which may affect patient health related problem , thereby increase days of hospital stay and costs.

Out of 32 prescriptions, 46.7% were male patients and 53% were female patients. Most of the patients were in age group above 70 years. This study describes some examples of major drug – drug interaction found during routine practice in surgical gastroenterology. In this study most frequent interaction was concomitant use of QT prolonging agents which increases the risk of QT interval prolongation. It could have a negative impact on patient safety. Some of these agents were given to increase motility as part of enhanced recovery programme The medication which were more frequently associated with QT interval prolongation were: ondansetron, domperidone, fluoroquinolones. Most of the major possible interactions were pharmacodynamics (91.25%) in nature. A common pharmacokinetic interaction found was orally absorbed cefuroxime with pantoprazole. Proton pump inhibitors may decrease the absorption of cefuroxime (oral).

The severity assessment of drug-drug interaction in our study showed 55.6% minor interaction followed by 23.7% moderate interaction and 20.6% major interaction. For patients

with less than or equal to 5 drugs prescribed per day have 28% interaction and patients with more than 5 drugs prescribed per day have 71% possible drug drug interaction.

Our study found that the average number of drugs prescribed per day in surgical gastroenterology is 11 and average length of stay in hospital was 10 days. Several other studies shows length of hospital stay and number of prescribed drugs have a positive association with drug -drug interactions.[12,13] This is similar to our findings as the number of drugs prescribed per day increases possible drug- drug interaction increases.

Management option for preventing drug-drug interactions:

- Avoid the combination entirely
- Adjusting the dose of the object drug
- Spacing dosing times to avoid interaction
- Close monitoring and early detection of interacting drug combinations
- Improve computerized drug interaction screening systems
- Consultation with clinical pharmacist provide latest potential drug-drug interaction and alternative therapies.

CONCLUSION

Significant drug to drug interactions do occur frequently in day to day practice in surgical units. Clinical pharmacists have a significant role in identification and controlling possible drug-drug interactions.

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Abbreviations Used

DDI: Drug-Drug Interactions

ADR: Adverse Drug Reactions

QOL: Quality Of Life

CONFLICT OF INTEREST

The authors hereby declare no conflict of interest.

SUMMARY

In future timely identification and reporting of drug-drug interaction by clinical pharmacist is essential as it reduce drug related problem and improve patient's QOL in hospital. Several measures such as better communication among patients, physicians and clinical pharmacist and de-prescribing can reduce polypharmacy and inappropriate therapy. Implementing such measures may reduce serious drug interactions when prescribing

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