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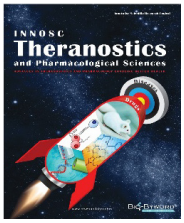

RESEARCH ARTICLE

Identification and Documentation of Potential Drug-drug Interactions in Inpatients at a Tertiary Care Center

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Abstract: ***Background:*** Drug-drug interaction (DDI) poses a marked risk to the patient's health outcome and puts an economic burden on health-care system.
Objective: The aim of the study was to determine the occurrence of potential DDIs and the association between the number of drugs and DDIs.
Methods: A prospective observational case study was conducted for the duration of 3 months from January 2014 to March 2014 in the Inpatient Department of General Medicine, General Surgery, and Orthopaedics of Gandhi Medical College and Hospital, Secunderabad. The patient demographic data were collected by designing a patient profile form and the DDIs were assessed and analyzed using the standard online health-care database.
Results: A total of 60 case sheets were analyzed. Of these 60 prescriptions, the potential DDIs showed with a majority being of moderate in severity 73.97% such as that of mannitol and ramipril being the most common drug interaction among the cases collected. At least one potential DDIs were observed in 36.66% of the prescriptions. Age and gender did not have any significant effect on DDIs.
Conclusion: Therefore, it was observed that DDIs in inpatients were frequent and pharmacist plays a crucial role in managing medication therapy of patients by collaborating with the health-care professionals to prevent adverse drug reactions. DDIs may not appear to cause a serious health problem to the patients and process of drug therapy, but clinical investigations are required to know the actual consequence of the DDIs.

Keywords: Drug-drug interactions, health outcome, prescriptions, polypharmacy, orthopedics.

1. INTRODUCTION

Drug interaction is defined as combining two or more drugs in a way that the potency of one drug is modified due to the presence of another drug [1].Drug interactions are said to occur when the pharmacological action of a drug is altered by concomitant use of another drug. The drug whose activity is affected by such interaction is called as the object drug and the agent which precipitates such interaction is referred to as the precipitant drug.

1.1 Factors Causing Drug-drug Interactions (DDIs) [2]

1.1.1. Multiple Drug Therapy

It is common in most acute and chronic care settings. Theoretically, the possibility for drug interactions to occur is over 50% when a patient is receiving five medications, and the probability increases to 100% when seven drugs are used.

1.1.2. Multiple Prescribers

Some individuals go to more than one physician, and it is common for a patient to be treated by one or more specialists in addition to a family doctor.

1.1.3. Multiple Pharmacological Effects of Drug

Most drugs used in the current therapy exhibit more than one type of pharmacological action and have the capacity to influence many physiological systems. Therefore, two concomitantly administered drugs will often affect some of the same systems, for example, antihistamines (secondary effect is sedation) enhance the sedative effect of tranquilizers.

1.1.4. Multiple Diseases/Predisposing Illness

Some patients take several drugs due to their suffering from more than one disease. Multiple therapies in such individuals generally result in drug interactions.

1.1.5. Poor Patient Compliance

This results when a patient does not take medication in the manner intended by the doctor, which may be due to inadequate instructions from the doctor or pharmacist, confusion regarding taking several medicines, etc., all of which may lead to either underdosing or overdosing, and a consequent drug interaction.

1.1.6. Advancing Age of Patient

Increased tendency of drug interaction episodes in the elderly is generally due to decrease in liver function in such individuals.

1.1.7. Drug-Related Factors

Clinically, significant interactions are most likely to occur between drugs that have potent effects, a narrow therapeutic index, and a steep dose-response curve.

Polypharmacy increases the risk of hospitalizations and medications errors. These factors result in increased patient cost, non-compliance to treatment, and increase in patient morbidity and mortality. Polypharmacy is classified as per the British National Formulary, which explains the concurrent use of 2–4 drugs as minor polypharmacy and the use of five or more drugs as major polypharmacy. Based on the knowledge obtained from this research, suggestions are to decrease the problems associated with polypharmacy as below:

- Patients should bring all their medicines to the counseling center
- Avoid on emergency self-medication
- Encourage physician in prescribing by following evidence-based medicine method
- The drug selected should treat more than one condition
- While prescribing a drug it should be checked for any contraindications and potential drug interactions
- The lowest dose must be selected and titrated as per the therapeutic effect observed
- Monitoring for adverse drug reactions must be done
- Patient education on drug therapy and the importance on medication use must be explained
- Patient compliance must be routinely checked and encouraged
- Therapeutic regimen must be simplified and any harmful drugs must be stopped or avoided
- Duration of drug use must be limited [3].

With the aim of the maintaining the low-cost quality health care, it is important to rationalize the drug use. The dispenser used for dispensing medications must be updated regularly with appropriate information, tools, and skills. Studies show that along with prescribed medication patients also adopt to self-medication.

Use of non-prescription drugs, self-medication could be beneficial to patients, health-care professionals, the pharmaceutical industry, and government only if these drugs are rationally used. For this, pharmacists play an important role in educating the patients on rational drug use as self-medication can lead to adverse effects of various severities [4]. The various types of drug interactions are DDIs, food-drug interactions, chemical-drug interactions, drug-laboratory test interactions, and drug-disease interactions.

Most of the drug interactions are types of adverse reactions with the altered efficacy of the drug, for example, enhancing the pharmacological activity (e.g. increase in hemorrhagic activity of warfarin when phenylbutazone is given in combination) or decreased therapeutic activity as in the case when tetracycline is coadministered with food, antacids, or mineral supplements containing heavy metal ions. Based on medications prescribed the DDIs are identified and classified.

The types of severity for the potential DDIs are classified as major: This can cause life-threatening or permanent damage to the patient, moderate: This can cause patients' clinical status to deteriorate or prolong his/her stay in hospital, and minor: This causes mild severity which is of less harm [5]. Therefore, the present study prompted us to conduct a research which was aimed at "Identification and documentation of potential DDIs in inpatients of a tertiary care multispecialty hospital."

2. MATERIALS AND METHODS

The study is a prospective, observational, and pilot research work which is done at an Inpatient Department of General Medicine, General Surgery, and Orthopedics of Gandhi Hospital, Secunderabad, during the study period from January 2014 to March 2014 for 3 months. It was aimed to identify and document the potential DDIs in inpatients at a tertiary care center. The inclusion criteria consisted of patients admitted in the inpatient departments of all ages and pregnant women, lactating mothers, and terminally ill patients, and outpatients were excluded from the study. For this purpose, data collection and documentation form were designed for incorporating patients' details. This format contained following details such as IP/OP number, date of admission, date of discharge, reason for admission, patient medical and medication history, vital signs, blood glucose levels, complete blood picture, liver function test, kidney function test, electrolytes, complete urine examination, lipid panel, diagnosis, and medication chart. Along with this, a DDIs documentation form was prepared to document various potential drug interactions observed in various case sheets. The study activities included a regular visit to the various inpatient wards followed by the documentation of cases on documentation form based on inclusion criteria. The collected data were thoroughly analyzed and the prescriptions were checked for DDIs using the standard health-care databases as Lexicomp and website as www.drugs.com.

3. RESULTS

Overall, a total of 60 cases were collected for study duration of 3 months. In our study, it was observed that out of 60 prescriptions, 13 (21.66%) were female and 47 (78.33%) were male. As per age-wise distribution, it was seen that 6 cases (10%) were within the age group up to 20 years. 40 (66.66%) cases were between 21 and 60 years and rest 14 (23.33%) above 60 years. Most of the cases collected comprised general medicine as 51 (85%), general surgery 6 (10%), and orthopedics 3 (5%).

Table **1** shows ward-wise distribution of potential drug interactions. The observed potential drug interactions consisted of 5 (6.85%), 4 (5.48%), and 64 (87.67%) in the general surgery, orthopedics, and general medicine wards, respectively.

A total of 73 potential DDIs were observed. Table **2** represents commonly occurring drug interaction combinations starting with mannitol and ramipril and ranitidine and acetaminophen occurring 6 times (8.2%) each, followed by ceftriaxone and furosemide 5 times (6.8%) and followed by ciprofloxacin and ondansetron; ondansetron and tramadol; and ranitidine and phenytoin occurring 3 times each (4.11%).

Table **3** shows that the number of potential DDIs is ranging from 1 to 7 where maximum numbers of seven DDIs detected in 1 (1.66%) prescription and the minimum DDIs detected were 1 in 22 (36.66%) prescriptions.

Table **4** depicts the severity of DDIs such as major (causes life-threatening or permanent damage to the patient), moderate (causes patients' clinical status to deteriorate or prolong his/her stay in hospital), and minor (causes mild severity which is of less harm). A total of 71 potential DDIs were reported.

Potential DDIs have seen to occur although most are not clinically significant. Patients with cardiovascular diseases and those who are prescribed multiple medications need to be monitored more closely.

To decrease the frequency of potential drug interactions, it is necessary to carefully select other therapeutic alternatives. In cases where no option of alternative therapy is available, continuous monitor for adverse events becomes mandatory.

4. DISCUSSION

Overall, 60 cases were collected and reviewed during the study duration of 3 months and the following interpretations were made from the observed data. Of these 60 prescriptions, 38 (63.33%) of the prescriptions showed the potential drug interactions. In our research work, we observed that male genders are more than female. This may be due to lack of awareness about the disease in female and male dominating society which prohibits female to go for treatment purpose. Socioeconomic burdens are also an important factor which limits female from treatment. This result was in comparison to the research work conducted by Legese *et al*., 2013 [6].

In this study, we found that maximum patients fall into the age group of 21–60 years which may be due to the factor that the physiological function starts deterioration from this age group. In addition to this, factors such as improper diet,

Table 1. Ward-wise distribution of drug-drug interactions (*n* = 71)

Ward	Number of drug-drug interactions	Percentage of drug-drug interactions per ward
General surgery	5	6.85
Orthopedics	4	5.48
General medicine	62	87.67
Total	71	100

Table 2. Most common drug-drug interactions

Drug combination	Number of cases	Severity	Consequences of drug-drug interactions	Percentage
Mannitol				
Ramipril	6	Moderate	Causes hypotension and hypovolemia	8.2
Ranitidine				
Acetaminophen	6	Minor	Potentiate the hepatotoxicity	8.2
Ceftriaxone				
Furosemide	5	Moderate	Potentiate the nephrotoxicity	6.8
Ciprofloxacin				
Ondansetron	3	Moderate	Causes hyperkalemia hypomagnesaemia	4.11
Ondansetron				
Tramadol	3	Moderate	5-HT_3 receptor antagonists reduce the analgesic efficacy of tramadol	4.11
Ranitidine				
Phenytoin	3	Moderate	Ranitidine increases the plasma concentration of phenytoin	4.11

5-HT3: 5-Hydroxytryptamine type 3

Table 3. Total number of drug-drug interactions occurred per prescription

Number of drug-drug interactions per case	Number of prescriptions (%)
0	22 (36.66)
1	22 (36.66)
2	6 (10)
3	7 (11.66)
5	1 (1.66)
6	1 (1.66)
7	1 (1.66)
Total	60 (100)

Table 4. Distribution of drug-drug interactions according to the degree of severity

Severity	Number of drug-drug interactions (%)
Major	4 (10.95)
Moderate	54 (73.97)
Minor	13 (15.06)
Total	71 (100)

lack of exercise, and social habits result in exacerbation of the condition, and the same has also been published previously by Magro *et al*., 2007 [7].

Of 60 cases, a total of 73 DDIs were identified and documented. From the documented DDIs, we found that most common were with mannitol and ramipril (6 cases) 8.2% and ranitidine and acetaminophen (6 cases) 8.2%. These data were found to be in comparison with the study carried out by Jimmy *et al*., 2012 [5], which showed the common drug interactions of furosemide with theophylline (16), followed by paracetamol with furosemide (15) and azithromycin with ondansetron (13).

In our study, DDIs per prescription varied from 1 to 7. In 22 cases, we found single DDIs per prescription. There were two and three DDIs per prescription also with the percentage of 10 and 11, respectively. Although negligible, it was found that there were DDIs as five, six, and seven per cases which are a matter of concern and should be encountered properly. Same was reported earlier by Jimmy *et al*., 2012 [5], which showed a total number of potential DDI from 1 to 10. A total of 42 cases (35%) showed a single potential DDI and 10 potential DDIs were seen in two cases each. Similarities were also found with a study conducted by Akshaya *et al*., 2013 [1], which reported 1324 DDIs of 711 drugs administered to patients from a total of 2180 prescriptions which contained two or more drug regimens. In five prescriptions, a maximum of nine DDIs were detected and one was the minimum DDI observed.

In our study, we found that most common DDIs are of moderate severity (73.97%) which can be overcome by keeping time space between coadministration of interacting drugs. A proper patient counseling and education by the health-care personal can overcome this situation. About 15.06% of cases of minor severity were also found in the study and considered to be adjusted DDIs which are common in the regular clinical practice. Our study can be compared with the results obtained from a study conducted by Jimmy *et al*., 2012 [5], which reported a total of identified DDIs to be 30 of which 82 of major severity (24.85%), 176 of moderate severity (53.33%), and 72 (21.82%) of minor severity.

Another study was conducted by Mylapuram *et al*., 2012 [8], reported 47 (9.92%) belonged to Level 1 significance which consisted of severe type, 201 (42.41%) of Level 2, that is, moderate, 72 (15.19%) of Level 3 which were minor severity from a total of 474 DDIs and which was in comparison to our study.

CONCLUSION

From our study, we conclude that potential drug interactions were present in prescriptions, of which drugs used to treat cardiovascular disorders were the common causative agents followed by analgesic, antacids, and antibiotics. Pharmacists play a major role in identification, documentation, and reporting of such potential DDIs to clinicians so that appropriate steps can be taken to overcome any further complications which may lead to rationalization of therapy and better patient care. This study can further be extended with more number of cases and for a longer duration to get a broad idea on the potential DDIs in various other departments with respect to the wide range of diseases encountered.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest in any kind.

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