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Study of Drug-Drug Interactions: A Potential Need for Safe And Effective Usage Of Drugs In A Teritiary Care Hospital

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Abstract: Objectives: The main objectives of the study was to identify and classify the drug-drug interactions based on their severity, Mechanism , Clinical Outcome and to identify the most frequently interacting drug combination for the departments of General Medicine, General Surgery, Gastroenterology, Orthopedics, Gynecology and Dermatology. **Methodology:** A prospective observational study was conducted for six months. The data of patients was collected and analyzed from inpatient departments of General Medicine, General Surgery, Gastroenterology, Orthopedics, Gynecology and Dermatology respectively. **Results:** A total of 250cases were observed and 150 cases containing Drug-Drug Interactions are considered for the study during the period of August-2016 to January-2017. Out of which 25 cases from each department were considered, analyzed and interpreted using Micromedex database. The prevalence of Actual DDI's was greater compared to the potential DDI's and was highest in the gastroenterology department. The prevalence of Moderate DDI's was highest compared to the Major DDI's and the prevalence of pharmacodynamic DDI's is highest when compared to the pharmacokinetic mechanism. A list of repeating combinations was prepared and it was observed that the combinations differ from department to department. **Conclusion:** From the study it can be concluded that most of the drug-drug interactions occurring were potential in occurrence, moderate in severity and usually would take place through Pharmacodynamic mechanism.

Keywords: Actual Drug-Drug Interactions, Potential Drug-Drug Interactions, Major, Minor, Pharmacokinetic, Pharmacodynamic.

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I. INTRODUCTION

Drug - Drug interactions are widely an important source of medication errors.[1]As the number of drugs in the prescription increases, the chance of occurrence of drug interactions also get increased.[2] Prescription containing 5 drugs has 40% and prescription with 7 or more than 7 drugs exceeding to 80% has incidence of potential drug-drug interactions.[3,4] Drug interactions vary depending on population type and environmental factors so, incidence of drug interactions is a controversial issue.[5] Drug-drug interactions are more likely to develop in hospital inpatients because of severe illness, comorbid conditions, polypharmacy, chronic drug regimen, frequent alterations in therapy.[6] The physiology of a patient changes as the age increases affecting the pharmacokinetics and pharmacodynamics features of many drugs leading to increased susceptibility of drug interactions in elderly people.[7] Possible way to prevent drug interactions includes viewing past medical history, pharmacological principles and by computerised screening systems for prescriptions which detects potential drug interactions.[8] Interactions affects the quality and socio-economic status of the patient.[9]

An interaction is said to occur when the effect of one drug is changed by the presence of another drug.[10]Potential drug interactions are identified on the basis of retrospective data and Actual drug interactions on the basis of clinical evidence (laboratory investigations and clinical symptoms).[11]Based on severity the interactions were classified into three groups namely Minor; Moderate; Major.[12] Narrow therapeutic index drugs, polypharmacy, disease state (Hepatic and Renal impairment) and environmental factors may lead to alterations in drug action.[13,14]

Physician should have awareness regarding interactions and should be able to recognise and prevent them. Occurrence of drug interactions can be reduced by identifying the risk factors and maintaining complete history of the patient, initiating alternative drug therapy whenever needed, individualize the therapy and patient

should be educated.[15] Physician should perform safety monitoring, effectiveness and evaluating patient response to therapy.[16]Patients condition should be monitored and if necessary, dosage adjustments and change in medication with less interacting properties should be prescribed.[17,18]Monitoring programs should be conducted for early detection and prevention of interactions to enhance quality of life.[19]

II. MATERIALS AND METHODS

This prospective observational study was conducted in the in-patient departments of General Medicine, General Surgery, Orthopaedics, Gastroenterology, Gynaecology and Dermatology in tertiary care hospital during August 2016 - January 2017. Prescriptions of patients are collected with necessary information according to inclusion criteria (above mentioned departments). Medico-legal, Paediatrics, Oncology and absconded cases were excluded. All the information was collected in well-designed data collection form. All the collected data was entered into MS-Excel. The raw data was analysed using the Micromedex database and Stockley's text book of drug interactions and they were classified into three groups based on clinical significance, severity and mechanism.The most commonly repetitively interacting drug combinations per department were listed. Descriptive statistics were used to describe the characteristics of the patients and number of Drug-Drug Interactions and their percentage prevalence per department.

III. RESULTS

During the study period of August 2016- January 2017 a total of 250 cases were reviewed and 150 casescontaining Drug-Drug Interactions were considered for the study which was found to have 279 Drug-Drug Interactions according to inclusion criteria. Out of which 25 cases from each department were considered.

Table 1: This table provides an outline of the whole study. Different DDI's have been observed in the tertiary care hospital and they have been classified based on different characteristics. Out of 279 drug-drug interactions, based on gender-145(51.9%) are male and 134(48%) are female, based on clinical outcome -59(21%) are actual drug interactions and 220(78.8%) are potential drug interactions, based on severity-46(16.4) are major drug interactions and 233(83.5%) are moderate drug interactions and based on mechanism- 102(36.5%) are pharmacokinetic drug interactions and 177(53.4%) are pharmacodynamic drug interactions.

Table-1: Classification of DDI's based on different characteristics**:**

		N	**%**
Total number of cases		150	100
Total number of Drug-Drug interactions		279	100
Classification based on Gender	Male	145	51.9
	Female	134	48
Classification based on Clinical Outcome	Number of Actual drug interactions	59	21
	Number of Potential drug interactions	220	78.8
Classification based on Severity	Number of major drug interactions	46	16.4
	Number of moderate interactions	233	83.5
Classification based on Mechanism of Drug Interactions	Number of pharmacokinetic drug interactions	102	36.5
	Pharmacodynamic drug interactions	177	63.4

Table 2: This table clearly demonstrates that the total number of Actual and Potential DDI's are higher in General Medicine.

Table - 2: Comparison of Actual and Potential DDI's among different departments

Department	**Actual (n)**	**%**	**Potential (n)**	**%**
General Medicine	22	26.1	62	73.8
General Surgery	11	25	33	75
Gastroenterology	9	34.6	17	65.3
Orthopaedics	8	17.7	37	82.2
Gynaecology	7	16.6	35	83.3
Dermatology	2	5.2	36	94.7

Table 3: The highest number of Major and Moderate DDI's are found in the general medicine(16)(68) department and the least are found in Gastroenterology(1)(25) respectively.

Table – 3: Comparison of Major and Minor DDI's among different departments

Department	Major (n)	%	Moderate (n)	%
General Medicine	16	19	68	80.9
General Surgery	7	15.9	37	84
Gastroenterology	1	3.8	25	96.1
Orthopaedics	9	20	36	80
Gynaecology	11	26.2	31	73.8
Dermatology	2	5.3	36	94.7

Table 4: The frequency of Pharmacodynamic DDI's is higher in all departments except for Gastroenterology where the Pharmacokinetic DDI's are 19 and the Pharmacodynamic DDI's are 7.

Table-4: Comparison of Pharmacokinetic and Pharmacodynamic DDI's among different departments.

Department	Pharmacokinetic(n)	%	Pharmacodynamic (n)	%
General Medicine	33	39.2	51	60.7
General Surgery	08	18.1.	36	81.8
Gastroenterology	19	73	07	26.9
Orthopaedics	17	37.7	28	62.2
Gynaecology	08	19	34	80.9
Dermatology	17	44.7	21	55.2

Table 5: Most of the departments contain Metabolism as the predominant mechanism of the Pharmacokinetic DDI's while Gynaecology (50%) has Distribution and Orthopaedics contains Absorption(52.9%). (A-Absorption, D-Distribution, M-Metabolism, E-Elimination)

Table – 5: Comparison of Pharmacokinetic Mechanisms among different departments

Department	A(n)	A(%)	D(n)	D(%)	M(n)	M(%)	E(n)	E(%)
General medicine	06	18.1	01	3.03	21	63.6	05	15.1
General Surgery	02	25	02	25	04	50	00	00
Gastroenterology	06	31.5	00	00	12	63.1	01	5.2
Orthopaedics	09	52.9	00	00	07	41.1	01	5.8
Gynaecology	01	12.5	00	00	03	37.5	04	50
Dermatology	00	00	00	00	17	100	00	00

Table 6: Among the Pharmacodynamic DDI's, The Synergistic mechanism is predominant in all departments except for Gastroenterology where the Antagonistic nature is high(71.4%).
(S-Synergistic, A-Antagonistic)

Table-6: Comparison of Pharmacodynamic Mechanisms among different departments

Department	S(n)	S(%)	A(n)	A(%)
General Medicine	47	92.1	04	7.8
General Surgery	36	100	00	00
Gastroenterology	02	28.5	05	71.4
Orthopaedics	26	92.8	02	7.1
Gynaecology	33	97	01	2.9
Dermatology	19	90.4	02	9.5

Table 7: This table illustrates the most commonly repetitively interacting drug combinations per department along with their effects.

Table-7: Drug-Drug Interactions combination per department.

Department	Combination	Effect observed in the patient
	Atenolol+ Diclofenac Atenolol+Amlodipine	Increased Sr.Creatinine Hypotension

General medicine	Atenolol + Furosemide Warfarin+ Heparin Ciprofloxacin+ Ondansetron Furosemide+ Metoprolol $Feso_4$ + Pantoprazole	Hypotension Bleeding QT interval Prolongation Hypotension Achlorohydria.
General Surgery	Ceftriaxone+ Amikacin Amikacin+ Diclofenac Ciprofloxacin + Amlodipine	Nephrotoxicity Nephrotoxicity Hypotension
Gastroenterology	Iron folic acid + Pantoprazole Tramadol + Ondansetron	Decreased absorption of Iron folic acid Agitation
Orthopaedics	Iron folic acid + Calcium Cefuroxime + Amikacin	Decreased absorption of Iron folic acid Nephrotoxicity
Gynaecology	Theophylline + Hydrocortisone Tramadol + Ondansetron	Hypokalemia Pain not subsided
Dermatology	Dexamthasone + Amlodipine Erythromycin + Hydroxyzine	Hypertension not subsided QT interval prolongation

IV. DISCUSSION

A total of 250 cases were observed and 150 cases containing Drug –Drug Interactions are considered for the study. Out of which 25cases from each department such as General Medicine, General Surgery, Gastroenterology, Orthopedics, Gynecology and Dermatology were considered , Analyzed and interpreted using Micromedex database and stockley's text book of drug interactions during the period of August -2016 to January 2017. Among those 150 cases 279 Drug-Drug Interactions were found and the descending order of Drug-Drug Interactions per department is as follows General Medicine, followed by Orthopedics, General Surgery, Gynecology, Dermatology and Gastroenterology. Which was in accordance with the study conducted by **Lubinga SJ**.[20]

Among the collected cases, Males were 72 (with 145 interactions) females were 78 (with 134 interactions). Yet the male predominance among drug Interactions has been observed, the Drug -Drug Interactions number was found to be higher in males when compared to females which was accordance with the study conducted by **Zaredar N**.[21]On the whole, the incidence of Moderate drug-drug interactions is higher compared to that of the Major drug-drug interactions which was in accordance with the study conducted by **Londhe SKP**. The incidence of Major Drug -Drug Interactions is highest in Gynaecology and least in Gastroenterology. Whereas the incidence of Moderate drug interactions is exactly opposite of that of the major drug-drug interactions.[22]The prevalence of Actual Drug-Drug Interactions was found to be less when compared to the potential drug-drug interactions which is in accordance with **Jimmy O.D. [**23]

The pharmacokinetic drug - drug interactions can be further divided into absorption, distribution, metabolism and elimination. The Absorption based Drug - Drug Interactions is highest in Orthopaedics due to the presence of combinations such as ferrous sulphate + Calcium which forms chelates and prevents the absorption of both the drugs. The Distribution based is highest in General Surgery. The metabolism based is highest in Dermatology and least in Gynaecology. The elimination based is highest in Gynaecology and least in Gastroenterology. Amikacin and Furosemide were mostly involved in interactions causing Nephrotoxicity whereas Tramadol was involved in interactions which lead to decrease in the Seizure threshold. Pantoprazole was involved in interactions which interfere with the Pharmacokinetic properties of other drugs.Most of the drug-drug interactions were found to occur through Pharmacodynamicmechanism which is in accordance with the study conducted by **Lopez VAS.**[24]The Pharmacodynamic drug - drug interactions are further classified into Synergistic and Antagonistic. The Synergistic based interactions are highest in Gynaecology and least in Gastroenterology.

It was found that the frequently interacting drug Combinations of the complete hospital are not in accordance with the most interacting combinations per department because the drugs commonly used were different from department to department.As per our findings there is a chance that the patient medication might contain a Drug Drug Interaction which may be **Potential in occurrence, Moderate in severity** and could occur through **Pharmacodynamic** mechanism which was accordance with the study conducted by **Zaredar N.**[21]

V. CONCLUSION

The high prevalence of potential Drug-Drug Interactions in most of the Departments is due to the presence of certain Combination which are followed in the hospitals. Hence these combinations should be altered. It was found that most of Drug Interactions occurring were Pharmacodynamic in nature and are moderate in severity and hence can be avoided with the change in the duration of administration. There is a lot of scope to develop new tools to assess the Drug-Drug interactions .One of the latest method to reduce the prevalence of Drug-Drug Interactions is to implement the Medication Therapy Management program where Pharmacists optimise the drug therapy of the patients and improve the therapeutic outcomes of the patients. Physicians can even be trained by providing them the list of most commonly interactions causing drugs in the hospital they work.

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