Incidence of Drug-drug Interactions in Prescriptions of General Practitioners and Specialists in Bangladesh

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Aim: Drug-drug interactions (DDI) can cause unexpected side effects, changes in drug efficacy, metabolism or overall action of any particular drug and DDI is one of the major prescription errors. DDI can be caused by using concomitant administration of a second drug. This study aims to find DDI in prescriptions of 10 different medical specializations of Bangladesh.
Study Design and Methodology: This study is based on the evaluation of prescription, type, and clinical significance of drug-drug interaction. For this study, 21088 prescriptions were evaluated from 45 different medical institutions and 10 different specializations including general practitioners, cardiologists, medicine specialists, general surgeons, gynecologists, ENT specialists, neurologists, urologists, pediatricians, and ophthalmologists. After the collection of prescriptions, all prescribed medications were checked by using several sources to point out the probable interactions.
Results: Among all the prescriptions most DDI was found from cardiologists (6.17%) and the least DDI was found from pediatricians (3.29%). Clopidogrel and warfarin were the most common medications causing drug interaction while drug interaction with cardiovascular drugs and

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antibiotics generic were most common among all. Polypharmacy, absence or shortage of pharmacists, workload, miscommunications and lack of knowledge were found as the leading causes of DDI.

Conclusion: Active participation of the pharmacist in crosschecking the prescribed medication, proper communication of the physician and patients, relevant workshops regarding DDI and distribution of the workload of the physicians in different levels can play a role in minimizing DDI.

1. INTRODUCTION

Drug-drug interaction (DDI) is recognized as one of the most frequent errors compares to other errors like, incorrect dose or medicine, duplicate therapy, incorrect route of administration, or wrong patient. It can cause far more complicated situations in patients of all ages [1,2]. DDI is characterized by the change in efficacy or toxicity of one drug (object) by prior or concomitant administration of a second drug (precipitant).

Both pharmacokinetic and pharmacodynamics properties of drugs can be altered as a result of DDI [3]. Pharmacokinetic DDIs mainly proceed with drug metabolism as over half of the drugs are metabolized by CYP3A4 [4]. However, absorption, distributions and excretion interactions involving transport proteins are also quite relevant. These can lead to either an increased or a decreased concentration of the drug. For example, carbamazepine is a strong inducer of CYP3A that can metabolize combined oral contraceptives and increase the risk of unwanted pregnancy [5]. Pharmacodynamics DDIs via additive, synergistic and antagonistic effects can change the efficacy or toxicity of the drug, without changes to its pharmacokinetics. Co-administration of dabigatran with verapamil increases bioavailability and the risk of bleeding [6,7].

The consequences of DDI affect patients not only physically but also economically. Every year a certain number of patients get admitted to the hospital due to these kinds of prescribing errors and the percentage is not ignorable (around 5%) [8]. These prescribing errors also reduce patient adherence, increase the patient's expenses, which can affect the whole society. The risk of DDI increased with polypharmacy. With increased number of medications, the chance of drug interaction also increases [9-11].

The number of drugs was given to the patients depends on several things including the severity of the disease, the patient's condition, and other clinical situations. So when patients have multiple symptoms, it requires more than a single drug. In this case, physicians need to consider the probability and possibility of DDIs [12,13]. Drugs with a low therapeutic index are more prone to DDI. The severity of illness and multiple disease conditions is also another prominent factor to DDIs, such as choosing medication for patients with cardiovascular disease and diabetes is quite difficult. Similarly, patients with infectious disease and psychiatric disorders have the greatest potential for dangerous drug interactions [14-16].

Drug interactions are one of the most important prescribing errors which can only be predictable and preventable by choosing drug very carefully with previous documentation, clinical reports, patients drugs history, and clinical studies. However, most physicians are not aware of different forms of DDI. Thus the aim of this study is to determine the severity of DDI, common DDI found in the prescription, consequences of DDI.

2. METHODS

The study was performed in Bangladesh. In this cross-sectional study, all data are collected from January 2018 to December 2020. Prescriptions were collected from 45 different medical universities, colleges, clinics, rural health complexes, and physician's chambers nationwide. All prescriptions included physician name, institution, strength, and quantity of the medications dispensed.

A total number of 21088 prescriptions were collected for the study. The prescriptions from 10 different medical specialists consisting of general practitioners, cardiologists, medicine specialists, general surgeons, gynecologists, ENT specialists, neurologists, urologists, pediatricians, and ophthalmologists. Prescriptions were collected from the patients with their consent. Only complete prescriptions were analyzed whereas incomplete and re-admission

prescriptions are omitted. The results of the DDI were analyzed by methods applied in the book Drug Interaction Facts. The book rated DDIs in a five-item summary measure based on the severity and corresponding report and documentation (probable, suspected, possible, and unlikely) for each drug interaction. Drug interactions are also checked using British Pharmacopeia, United State Pharmacopeia, and with the help of some free online websites including drugs.com interaction checker, Medscape interaction checker, and WebMd interaction checker.

3. RESULTS AND DISCUSSION

During the study a total of 21088 prescriptions were analyzed from January 2018 to December 2020. Among the data, a number of 3554 prescriptions are collected from the general practitioners, and the rest of the numbers are collected from other specializations. (Table 1) Nearly Six and a half percent of the total prescription had moderate DDI and more than four of the total prescription has severe DDI. In count, all prescriptions occurrence of moderate DDIs found mostly in cardiologists and medicine specialist whereas pediatricians were in the bottom. The average numbers of items found in the prescriptions are quite high, above 5. Among the practitioners, cardiologists (6.17) and medicine specialists (5.72) provided more medications compared to others, while pediatricians were at the bottom of the list with

an average of 3.29 items per prescription. (Table 2) The prescriptions that were collected are abandoned with antibiotics and anti-ulcer medications. Almost four third of the prescriptions contain these medications and almost half of the prescriptions contain cardiovascular drugs. (Table 3) The list of medications named in (Table 4) indicates that Diuretics, Clopidogrel, warfarin, and digoxin were the most common three drugs that were involved in drug-drug interaction. The study also revealed that drug interaction with cardiovascular drugs and antibiotics generic were most common among all (Table 5).

The study provides some information that there is some relation between the number of prescriptions and the occurrence of a drug interaction. That's why polypharmacy is an important factor that can lead to DDIs. As more the number of medications in prescriptions, the more the chances of DDI's occurrence [17,18]. Sometimes aggressive marketing plans by pharmaceutical companies influence polypharmacy [19]. Among all practitioners, cardiologists are prone to write more items in a single prescription, above six-item per prescription, and the occurrence of DDIs was also high compare to others. The same thing can be applied to general practitioners and medical specialists also. Some past studies on primary care indicate that the rates of potential DDIs for patients receiving two or more drugs were 24.3%, 29.5%, and 42.0%, respectively [20,21].

Table 1. Analysis of Prescription

Prescription	Number of prescriptions	% Moderate Interactions	Number of Prescriptions	% of Severe Interaction	Number of Prescriptions
All Practitioners	21088	6.473	1365	4.339	915
General Practitioners	3554	8.301	295	5.234	186
Medicine Specialists	2789	7.350	205	4.733	132
Cardiologists	2687	10.681	287	6.662	179
Pediatrician	1908	3.407	65	2.149	41
General Surgeons	1887	5.511	104	4.557	86
Ophthalmologists	1829	4.046	74	3.226	59
ENT Specialists	1733	5.597	97	2.193	38
Neurologists	1579	3.357	53	2.977	47
Urologists	1650	3.697	61	3.333	55
Gynecologists	1472	8.424	124	6.250	92

Table 2. Mean number of items per prescription

Specialization	Number of Items per prescription
All Practitioners Combined	5.04
Cardiologists	6.17
Medicine Specialists	5.72
ENT Specialists	5.59
General Surgeons	5.41
Neurologists	4.93
Gynecologists	4.88
Ophthalmologists	4.86
General Practitioners	4.75
Urologists	4.66
Pediatricians	3.29

Table 3. Abundance of Drug Categories in the drug interaction

Drug Categories	% Incidence per total of Prescriptions
Antibiotics	76.12
Antiulcerants (Anti-GRED)	72.75
Cardiovascular	44.58
ACE inhibitors	40.19
CNS drug	33.67
Diuretics	23.48
Antihypertensive	20.44
Analgesics	19.42
Antipyretics	15.28

Table 4. List of common drug interacting medication

Medication
a. Diuretics
b. Clopidogrel
c. Warferin
d. Digoxin
e. Salbutamol
f. Calcium
g. Azithromycin
h. Atenolol
i. Zinc
j. Ranitidine

Table 5. The result of investigation of major DDIs

Drug 1	Drug 2	Severity	Onset	Number
Digoxin	Furosemide	Major	Delayed	182
Azithromycin	Lovastatin	Major	Delayed	177
Azithromycin	Atovastatin	Major	Delayed	156
Ranitidine	Cefuroxime	Major	Delayed	149
Clopidogrel	Esomeprazole	Major	Delayed	146
Chlorpromazine	Propranolol	Major	Delayed	133
Aspirin	Warferin	Major	Delayed	127
Diclofenac	Prednilone	Major	Delayed	104
Propranolol	Verapamil	Major	Rapid	98
Atenolol	Verapamil	Major	Rapid	89

There are a bunch of reasons for medication errors by physicians. Some studies suggested that most mistakes by the physicians were made because of lack of attention, or physicians did not apply relevant rules for providing prescriptions. There are some other risk factors like the work environment in the prescribing area, workload, miscommunication with the patient, the mental condition of the physician, and lack of knowledge [22,23].

Pharmacists are the health professionals who play a vital role against several prescribing errors including medication errors. If this role is neglected the chance of prescribing errors surely increases. They provide overall scrutiny to the prescriptions and also monitor prescriptions to detect any kind of error that arises [24,25]. In the current time, there are very few hospitals and clinical pharmacists are working with the hospitals and healthcare providers. In this study we found only 6 institutions having hospital or clinical pharmacists out of 45 institutions. For that reason, a huge number of prescriptions went out to the patients without having a minimum check by pharmacists. The absence and shortage of pharmacists in Bangladesh means that their monitoring role is compromised. It may be one of the main reasons for having such huge DDIs in the prescription. A bunch of studies done previously on the consultation time of the patients with physicians in this country. The average consultation time was very low (average 2.33 min) [26-28]. This minimum time is always helpful for choosing the perfect number and choice of medication, which also can be lead to prescribing errors and potential DDI.

4. CONCLUSION

Potential drug-drug interactions are most frequent among outpatients prescribed multiple medications. Polypharmacy is directly related to drug interaction and medication error. In a nutshell, it is our opinion that physicians need to pay cautious attention to DDIs, especially cardiovascular drug prescribers. Active participation of pharmacist, need to be ensured in the healthcare institution. Moreover, to improve knowledge, participating error related workshops should be arranged for prescribers.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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