Original Article

Assessment of Drug-Drug Interaction in Selected Community Pharmacies

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ABSTRACT

Studies have reported that there is a high prevalence of potential DDIs in prescriptions dispensed in community pharmacies. The problem is made even more complex by the concomitant use of over-the-counter medications. This study aimed to evaluate the nature, type, and prevalence of potential drug-drug interaction in prescriptions dispensed in community pharmacies. A prospective observational study was conducted, all 1,010 prescriptions dispensed in the three community pharmacies in 6 months were collected. Using MICROMEDEX®'s Drug Interactions Checker, potential DDIs were identified. 1010 prescriptions were analyzed, out of which the majority of the participants belonged to the age group of adults (72%) followed by geriatrics (21%). The prescriptions had the highest of moderate interactions with 45.83%, followed by major of 33% and 25% of minor interactions. In most prevalent drug drug interactions were ciprofloxacin and diclofenac with 29%, followed by paracetamol and domperidone being 12.5%. 9% were of Pharmacokinetic interaction and 91% were of Pharmacodynamic interaction. Overall, 120 prescriptions had one or more potential DDIs and a total of 95 major and moderate DDIs were identified. Major DDIs were identified in 3.9% of all prescriptions and represented 33.33% of all DDIs detected, whereas moderate DDIs were identified in 5.44% of all prescriptions and represented 45.83% of all DDIs detected. Ciprofloxacin, which interacts with Diclofenac (29.16%), was the most often involved drug in serious DDIs, followed by Paracetamol with Domperidone (12.5%). While it might not be possible to eliminate potential drug-drug interactions (DDIs) based on the need for polypharmacy, particularly in patients with multiple chronic diseases, healthcare providers must use all available educational resources to guarantee that the benefits of drugs always outweigh the risks for each patient increased with prescription size.

Keywords: Drug interaction, adverse drug reaction, Community pharmacies, prescriptions, severity.

INTRODUCTION

Drug-drug interaction (DDI) is a specific type of adverse drug event; it occurs when the effect of one drug is changed by the presence of another drug, resulting in increased toxicity or reduction in therapeutic efficacy. It has been shown that these events increase with patient age, with the number of drugs prescribed, and when multiple physicians are involved in patient care. [1] There is a high prevalence of potential DDIs in prescriptions dispensed in community pharmacies. The problem is made even more complex by the concomitant use of over-the-counter medications and certain types of food, ethanol, and smoking.

The most important mechanisms for drug-drug interactions are the inhibition or induction of drug metabolism, and pharmacodynamic potentiation or antagonism. Interactions involving a loss of action of one of the drugs are at least as frequent as those involving an increased effect. For those interactions that have come to clinical attention, it is important to review why they happened and to plan for future prevention. [2] Their prevention remains however complex in clinical practice as the number of drugs that can potentially interact is high. [3,4] Patients using multiple drug therapies are at a greater risk of being predisposed to AEs associated with drug-drug interactions (DDIs).[5] Depending on studies, DDIs are estimated to cause 2–5% of hospital admissions in elderly patients. DDIs are highly prevalent in older people as a result of multimorbidity, polypharmacy, and age-related changes in pharmacokinetics and pharmacodynamics that increase the complexity of therapeutic management, and treatment by multiple care providers.

The wide variance in DDI prevalence estimates is a consequence of the considerable heterogeneity in definitions and methods used to identify DDIs, in study populations and study settings.[6,7,8] And 1% of hospital admissions in the general population. Pharmacists can contribute to the detection and prevention of drug-related injuries, especially of clinically meaningful DDIs that pose a potential risk to patient safety. [9] In the Harvard Medical Practice Study of adverse events, 20% of events were drug-related. Of these, 8% were considered to be due to Drug-Drug Interactions (DDIs). In a study on the admissions of two hospitals in Britain, it was reported that adverse drug reactions were responsible for a significant proportion of admissions and drug interactions accounted for around 16% of adverse drug reactions resulting in hospital admissions. [10] DDIs can lead to complications, which in turn may prolong the length of hospital admission or even lead to death. [11] Some factors such as administration of drugs with low therapeutic index, severity of underlying diseases, and patient's age (commonly elderly) could increase the potential of dangerous drug interactions. Among medication errors, drug interactions could be easily prevented. [12] Although drug interactions are reported, there is no published report of the prevalence of such in ADEs related to drug–drug interactions increase the length

of stay in the hospital, add costs, and result in adverse consequences for patients. Many drugs have even been withdrawn from the market due to their potential to cause fatal drug–drug interactions. Most of the existing studies on DDI incidence focus on interactions in hospitalized patients, with fewer concerning the incidence of DDIs in primary care outpatients. DDI incidence estimates vary markedly across studies from different countries since the healthcare environments and systems vary. Drugs that are approved and marketed vary by country, and so do prescribing patterns. There are also big differences between drug interaction screening programs and databases about inclusion, severity classification, and documentation level of DDIs. Even widely used interaction screening programs differ in detecting interacting drug–drug pairs. These differences produce markedly varying results across the DDI incidence studies. [13]

This study aims to assess the prevalence of pDDI among patients presented to a community pharmacy in Bellur.

METHODOLOGY

A Prospective and Observational study is conducted in selected community pharmacies namely, Mahaveera Medicals, Cheluva Store & Fathima Medicals in and around Bellur, B.G Nagara.

1 Data Collection Tools: Prescription of patients at community pharmacy

Method of collection of data

1. Data collection forms

2. Patient interview

2 Study Approval

The study was approved by the Institutional Ethical Committee, AH&RC, B.G.Nagara

(No. IEC/AH&RC/AC/013/2022).

3 Study Criteria

The study was carried out by considering the following criteria

Inclusion Criteria: All valid medical prescription of patients who agrees to participate in the study.

Exclusion criteria: Medical prescription of patients who refuse to participate in the study.

4 Study Procedure

The study was conducted in Bellur B G Nagar which included three community pharmacies. Although there were 10 pharmacies selected, it was screened down to 3 pharmacies based on the patient rush and prescription availability. The three pharmacies included were contacted through the means of respective in-charge pharmacists using permission letters seeking appointments followed by a valid discussion with the co-pharmacist of the respective pharmacies.

Subjects were enrolled according to the inclusion and exclusion criteria along with the written consent form from each participant, the participants were allowed to decide on the participation and withdrawal from the study.

Suitably designed questionnaires for the data collection were used. The data collection process was done with the proper explanation of the aim of the study and questionnaires. The obtained data was subjected to suitable statistics and the results obtained were arranged according to the relevancy of the topic and objectives of the study.

Three community pharmacies were selected to obtain a representative sample of the population of community pharmacies. All 1,010 prescriptions dispensed in these three community pharmacies through 6 months were collected. Each participating pharmacist, following oral & written consent by the patient, confidentiality of all personal data from each prescription, including the patient's name, address was maintained and the information collected included age, gender, date of the prescription, diagnosis, specialty of the prescribing physician, name of the medications in each prescription, dosage, and quantity of medications dispensed. Using MICROMEDEX®'s Drug Interactions Checker, potential DDIs were identified. The detected DDIs were classified as major, moderate, and minor, depending on their severity of clinical significance, and cross-over was checked manually for the presence of enough published scientific evidence for the identified interacting agents. Major interactions are either well documented and have the potential of being harmful to the patient, or have a low incidence of occurrence (and perhaps limited documentation) and have the potential of serious adverse outcomes. Moderate interactions are of moderate clinical significance, are less likely than major interactions to cause harm to the patient, or are less well documented.

Minor interactions are of minor clinical significance. These interactions, regardless of the degree of their documentation, are the least significant because of limited risk to the patient. Due to interpatient variability, an interaction labeled as major may produce no harmful effects in some

Patients, whereas a moderate interaction can have serious negative consequences. Data was further analyzed statistically using Microsoft Excel.

RESULTS AND DISCUSSION

A total of 1010 prescriptions were analyzed during the study period from the community pharmacies for DDI, Prescriptions with single drug interactions were found to be high at 89% (n=107) followed by two drug interactions at 10% (n=12), three drug interactions 0.83% (n=1).

While assessing the severity of the drug interactions, 33% were major, 55% were moderate, and 25% of the interactions were minor which can be compared with the results obtained by Jacqueline M et al.6 where the major,

moderate, and minor DDIs were 17%, 56%, and 27% respectively and also similar to the results of Satish A et al.7 where major was 25.82%. [14]

Table 1: Distribution of DDI According to the Degree of severity

Distribution of DDIs according to the degree of severity		
Severity of DDIs	No. of DDIs	Percentage of DDIs
MAJOR	40	33.33%
MODERATE	55	45.83%
MINOR	25	20.83%
Total	120	100

Table 1 shows that the prescriptions had the highest of moderate interactions with 45.83% followed by the major of 33% and 25% of minor interactions.

The DDIs could be classified as pharmacokinetic (e.g. altered plasma concentration of drug) and pharmacodynamics outcomes. The study prescriptions comprised 9% pharmacokinetic, and 90.83% were pharmacodynamic outcomes. which is similar to the study conducted by Virendra K.P et al. The total PD interaction, had 45.45% of Absorption, 27.27% of Distribution, 18.18% of Metabolism & 9% of Excretion interactions where as in PD interaction, it had 68.8% of Synergism 12.8% of Antagonism & 18.34% Additive effect interaction.

Table 2: Types of pk interaction

Types of PK interaction	Frequency	Percent
Absorption	5	45.45
Distribution	3	27.27
Metabolism	2	18.18
Excretion	1	9.09

Table 2 shows types of PD interaction, it has 45.45% of Absorption, 27.27% of Distribution, 18.18% of Metabolism & 9% of Excretion interactions.

The most common interactions reported were with ciprofloxacin and diclofenac, while in the case of Jimmy O.D et al. Furosemide and theophylline had the most interactions, since in community pharmacies people come for minor cases like pain & infection ciprofloxacin and diclofenac are the most prescribed drugs followed by paracetamol and domperidone.

The documentation of 120 identified DDIs was fair (49%), (41.66%) DDIs were good and (9.1%) DDIs were excellent which is comparable to the study conducted by Joice MCS et al. [15] The DDIs were documented by referring to the literature for the combination of drugs prescribed. The studies carried out by Rajesh R et al., Reimche L et al., and Margro L et al., dealt with only potential interactions rather than genuine ones as they did not determine the clinical relevance of the interactions. [1617]

Table 3: Distribution of DDIs depending upon their documentation

Distribution of DDIs depending upon their documentation		
Type of Documentation	No. of DDIs	Percentage of DDIs
Fair	59	49.16%
Good	50	41.66%
Excellent	11	9.16%

Table 3 shows the distribution of DDIs depending upon their documentation, it had 49% of fair documentation followed by 41% of good documentation and 9% of excellent documentation.

The majority of the interactions were moderate 55%. There are many potential drug-drug interactions but they may not be seen in the patient clinically such as pharmacokinetic outcomes where the interaction may not precipitate to show the outcomes by visual appearance.

As stated by Janchawee Bet al, drug-drug interactions often need not always have clinically important adverse consequences but it is important to identify the DDIs in patients to prevent any possible harm to them. [18]

The identified DDIs were classified according to their severity, as major (the interaction may be life-threatening and/or require medical interventions to minimize or prevent serious adverse effects) and moderate (the interaction may result in an exacerbation of the patient's condition and/or require an alteration in therapy). [9] The findings highlight the need for a more effective and trustworthy DDI screening mechanism and provide an indicative picture of the issue with DDIs in prescriptions filled in community pharmacies. Physicians are now strongly advised to use electronic prescriptions, bar codes to help identify patients and their medications, an accurate system that provides new scientific evidence, and careful medication selection, among other recommendations. [19] Additionally, chemists play a crucial role in spotting and averting possible drug-drug interactions in patient prescriptions. [9] Limitations of this study were related to a certain degree of underreporting of potential DDIs because DDIs were detected only within one handwritten prescription and not reflecting a history, as well as without taking into account over-the-counter medications and herbal preparations (e.g., St. John's wort) which may contribute to DDIs.

It is known that DDIs can compromise therapy, for example, by increasing the length of therapy, and therefore specific measures that can ensure that healthcare professionals increase their awareness/recognition of potential DDIs may improve the quality of health care. [20]

To reduce the risks of drug interactions for patients, doctors, and chemists may find it helpful to have easy

access to drug interaction databases like Micromedex.com. These databases can help identify possible drug interactions throughout the prescription writing and dispensing process.

To guarantee that the best medications are provided, this would need to be paired with pharmacological competence, patient-specific information, and careful observation. Physicians can reduce risk or prevent adverse events (AEs) by selecting appropriate alternatives for major potential DDIs and by closely monitoring patients for moderate and minor possible DDIs.

While it might not be possible to completely remove potential drug-drug interactions (DDIs) based on the requirement for polypharmacy, particularly in patients who have many chronic diseases, healthcare providers have to consider the benefits and risks of prescribing and administering medications. When prescription medications have the potential to have side effects, the chemist may advise patients about the warning signs and symptoms that they may encounter and may strongly advise them to get medical help right away if these symptoms appear. One study limitation is that patients whose prescriptions contained possible drug-drug interactions were not immediately followed up with. [9]

Polypharmacy is a pivotal agent which leads to DDIs, the more drugs per prescribed orders, the more the probability of drug-drug interactions occurrence. [20] Our study confirmed that almost all prescriptions had 3-4 drug items per written order (an average of 3 items per prescription). Compared to our Studies, Iran's healthcare provider settings have reported that the mean items of drug per written order were 3.2 in 2007; however, it is decreasing but is at a standstill higher than other regions in the world with an average of 1.3-2.1 items per prescription. [20] Correspondingly, according to the results of some studies, the occurrence of potential drug interactions for patients receiving more than two drugs ranges from 24.3% to 42% therefore, the greater the number of drugs, the higher the possibility of DDIs.[20]

CONCLUSION

- Overall, 120 prescriptions had one or more potential DDIs and a total of 95 major and moderate DDIs were identified.
- The most common drug involved in major DDIs was Ciprofloxacin which interacts with Diclofenac and Paracetamol with Domperidone, this may be due to a lack of awareness of the prescriber and also due to common prescribing patterns from a long time without updating with latest information.
- The results of our study suggest that patients in Bellur may be at risk of adverse drug reactions (ADRs) as a result of potential DDIs. However, the study did not identify factors that influence drug interactions at the pharmacy level; potential causes include inadequate knowledge of DDIs or patient medication histories, as well as a lack of communication between primary and secondary healthcare providers or between prescribers and patients. Drug interactions may therefore be decreased by following the proper procedures for writing prescriptions, cutting down on the quantity of drugs prescribed, and raising doctors' awareness of potentially dangerous drug interactions, for instance, by enrolling in relevant educational courses.
- Lastly, it should be noted that DDIs are frequently experienced by patients who fill prescriptions at community pharmacies that contain multiple drugs. Pharmacists can help detect and prevent drug-related injuries as well as lower the rate of DDI and its associated hazardous consequences. Appropriate surveillance systems for monitoring drug interactions should also be put in place.
- While it may be impossible to eliminate potential DDIs based on the need for poly-pharmacy especially in patients with multiple chronic diseases, it is the responsibility of healthcare professionals to use all education tools available to ensure drug benefits always outweigh risks for each patient.

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