Pilot Study: Assessment of Drug-Food and Drug-Drug Interactions in the Outpatient Settings

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Authors’ contributions

This work was carried out in collaboration among all authors. Author NJA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors FZA and MFK managed the analyses of the study. Author NJA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: A drug-drug interaction arises when the pharmacologic effect of a medication is changed by the action of other medication causing unexpected clinical effects. Drug-drug interactions are widely known but the identification of the consequences of food and drug interactions has been growing slowly.

Aim: The present study aims to describe the occurrence of drug–food and drug-drug interactions in the outpatient settings in Riyadh city.

Methodology: A retrospective study was piloted in Riyadh city. The prescriptions were reviewed to identify potential drug - food and drug-drug interactions using Drug Interactions Checker.

Results: About 16.16% of the prescriptions included a drug - drug interaction. The most frequent interaction was the interaction between ciprofloxacin and metronidazole (25.00%) that is a minor interaction. Regarding drug – food interactions there were 40 interactions, the majority of these interactions were moderate. The most common drug - food interactions were metronidazole with food (20.00%) that is a major interaction.

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1. INTRODUCTION

An increased attention has been implemented to problems linked to drug prescription in the preceding years since adverse events are frequently seen and they result in a potential harm to the patients [1]. Pharmacological interactions are a main element of drug-related adverse events and remain one of the problems that could be prevented in clinical practice [2,3]. These adverse events are defined as the effect that is caused by the concurrent administration of two drugs and leads to a quantitative or qualitative change of therapeutic effect [4]. The drug–drug interactions could be actual if they are occurred or potential drug–drug interactions that could supposedly take place when two or more medications are given to a patient [5].

A drug-drug interaction happens when the pharmacologic effect of a medication is changed by the action of another medication causing unexpected clinical effects [6]. Drug-drug interaction is becoming a serious safety issue as the usage of numerous medications becomes more common. Drug-drug interactions are responsible for more than 30% of all adverse drug events [7,8]. In 2007, drug interactions resulted in about 0.57% of hospital admissions, 0.12% of re-hospitalizations and 0.054% of emergency department visits in the United States [9]. Cascorbi stated that the interactions between drugs can lead to serious unwanted effects or to a reduction in the therapeutic effects of some drug substances [10].

The effect of medication on an individual may be unexpected because that medicine interacts with dietary supplements the person is consuming, another medicine the person is taking, food, beverages or another disease the person has. A drug interaction leads to altering of drug activity, either decreased or increased, the interactions also may cause a different effect that neither produces on its own [11].

The drug interactions could make a clinically relevant effect in presence of medications with a long half-life, a low therapeutic index or a higher bound with plasma proteins [12]. It is essential to know the interactions and their causes to avoid them. Bertsche et al. reported that a computerized clinical decision support system was very successful and lead to reduce the interactions number from 66% to 54% and undesirable events number from 44% to 25% [13]. Additionally, post-marketing surveillance or pharmacovigilance is used nowadays to detect and quantify the risks related to the medications usage, thus contributing to better understand the main characteristics of adverse drug reactions and the pathogenic mechanisms involved [14]. Drug-drug interactions are well known but the recognition of the effect of food and drug interactions has been growing much slower [15].

It is important to know drug - drug interactions and drug - food interactions to implement the appropriate intervention that is required to treat patients efficiently. Therefore, this study aims to describe the occurrence of drug –food and drug-drug interactions in the outpatient settings in Riyadh city, Saudi Arabia.

2. METHODOLOGY

A retrospective study was conducted in Riyadh city, Saudi Arabia. The medical prescriptions were reviewed to identify potential drug–drug and drug - food interactions using Drug Interactions Checker that is available at https://www.drugs.com website [16]. The data were collected from the prescriptions that were prescribed in a community pharmacy and contain more than one drug, so the prescriptions that contain only 1 drug were excluded. There were no any demographic or personal data in the study and no competing interests exist.

The interactions between drugs with drugs and with food were classified as major, moderate, minor according to the level of significance. Moreover, the interaction was sometimes classified as a duplication.

The duplication could be type 1, 2 or 3. Type 1 means overlapping prescriptions of the same active ingredient in the same dosage form and with the same strength. Type 2 means

Conclusion: Drug interactions with other drugs or with foods are common. These interactions could have a beneficial or a harmful effect. Physicians and pharmacists should use programs that detects the drug interactions.

Keywords: Drug-drug interactions; drug–food Interactions; outpatient.
overlapping prescriptions of the same active ingredient but in a different dosage form, in a combined preparation with another active ingredient or in different strength. Type 3 means overlapping prescriptions of two different active ingredients belonging to the same therapeutic or pharmacological class [17].

3. RESULTS AND DISCUSSION

A sample of 99 prescriptions was collected from a community pharmacy in Riyadh city, Saudi Arabia to be checked for the presence of drug interactions. Out of the 16 interactions, no interaction was classified as a major (0.00%). The drug – drug interactions number was shown in Table 1.

Table 1. Number and percentages of Drug – Drug Interactions in the prescriptions

| Type of interaction | Number | Percentage |
|---------------------|--------|------------|
| Major               | 0      | 0.00%      |
| Moderate            | 5      | 31.25%     |
| Minor               | 6      | 37.50%     |
| Duplication         | 5      | 31.25%     |
| Total               | 16     | 100%       |

Out of 99 prescriptions, 16 prescriptions include a drug – drug interaction (16.16%). Karas et al. reported that the incidence of interactions was 16% in their study [18]. Farooqui et al. reported that in the 211 prescriptions collected from outpatient setting, a total of 369 drug-drug interactions were identified (175%) [19]. Khandeparkar and Rataboli stated that potential for drug-drug interactions was present in 94% of prescriptions with polypharmacy [20].

In contrast to the result of the previous study, Ahmed et al. reported that the prevalence of drug – drug interactions is high among patients in the outpatient settings and that the majority of the drug – drug interactions were of moderate severity [21]. Ahmed et al. also reported that out of 800 prescriptions, 290 have at least one drug-drug interaction (36.25%) [21]. Medina-Barajas et al. reported that most of the interactions in their study were minor [22]. They also stated that about 42% of the patients presented some degree of potential drug-drug interactions [22].

The most common interaction in this study was the interaction between ciprofloxacin and metronidazole (25.00%) that is a minor interaction. The most common interactions were shown in Table 2.

In the present study there were 5 duplication interactions, 4 were classified as a type 3 (overlapping prescriptions of two different active ingredients belonging to the same therapeutic or pharmacological class) and only 1 interaction (diclofenac - diclofenac topical) was classified as a type 2 (overlapping prescriptions of the same active ingredient, but in different dosage form).

The interactions between metronidazole and ciprofloxacin resulted in slightly more potent effect for treating infections caused by clostridia than ciprofloxacin or metronidazole alone [23]. The combination of ciprofloxacin with metronidazole is an antibiotic regimen that was recommended for the management of community-acquired abdominal infections in adults by the Infectious Diseases Society of America [24].

Regarding drug – food interactions there were 40 interactions, the majority of these interactions were moderate. The number and percentages of drug – food interactions are shown in Table 3.

Table 2. The most common drug – drug interactions

| Interactions                   | Number | Type       |
|-------------------------------|--------|------------|
| Clozapine – Paroxetine        | 2      | Moderate   |
| Ibuprofen – Metformin         | 1      | Moderate   |
| Atorvastatin – Esomeprazole   | 1      | Moderate   |
| Albuterol – Pseudoephedrine   | 1      | Moderate   |
| Ciprofloxacin – Metronidazole | 4      | Minor      |
| Cyanocobalamin - Esomeprazole | 1      | Minor      |
| Amoxicillin – Azithromycin    | 1      | Minor      |
| Ranitidine – Pantoprazole     | 1      | Duplication|
| Diphenhydramine – Loratadine  | 1      | Duplication|
| Ibuprofen - Diclofenac        | 2      | Duplication|
| Diclofenac - Diclofenac topical | 1     | Duplication|
The most common drug – food interactions were metronidazole with food (20.00%) that is a major interaction followed by the interaction between loratadine and food (15.00%) that is a minor interaction and ciprofloxacin food interaction (10.00%) that is a moderate interaction. Metronidazole may occasionally trigger a reaction in some patients similar to the disulfiram reaction if it is used with the consumption of alcoholic beverages or products containing propylene glycol or alcohol [16]. Taking ciprofloxacin with dairy products could make the medication less effective [16].

The most common drug – food interactions are shown in Table 4.

The most common drug – food interactions were metronidazole with food followed by the interaction between loratadine and food and ciprofloxacin food interaction.

Finegold reported that patients should avoid consuming alcohol or other products that contain propylene glycol during metronidazole use and within three days of therapy completion. Additionally, if there has been recent disulfiram use within the past two weeks, metronidazole is also contraindicated [25]. Bushra et al. stated that antihistamines interact with food and to increase the effectiveness, it is best to take these drugs on an empty stomach [11].

The absorption of ciprofloxacin is decreased if it is taken with milk due to the presence of casein and calcium [26]. Akinleye et al. reported that the effect of interaction of some fruit juices on the absorption and dissolution profiles of ciprofloxacin pills were determined and that it was found that the absorption of ciprofloxacin can be decreased by simultaneous consumption of grape fruit juice [27].

The most important interactions between drugs and food are those interactions associated with a high risk of therapeutic failure causing from a highly decreased bioavailability in the fed state. These interactions are caused commonly by chelation with food components. Furthermore, the physiological response to food intake particularly gastric acid secretion may decrease or increase the bioavailability of numerous medications [28,29]. To avoid such interactions, it is important to take the drug 2 hours after or 1 hour before eating [11].

Table 3. Number and percentages of drug – food interactions in the prescriptions

| Type of interaction | Number | Percentage |
|---------------------|--------|------------|
| Major               | 11     | 27.50%     |
| Moderate            | 21     | 52.50%     |
| Minor               | 8      | 20.00%     |

The most common drug – food interactions are shown in Table 4.

Table 4. The most common drug – food interactions

| Interactions      | Number | Type   |
|-------------------|--------|--------|
| Hydrocodone – Food| 1      | Major  |
| Metronidazole - Food| 8     | Major  |
| Metformin - Food  | 2      | Major  |
| Ciprofloxacin - Food| 4     | Moderate|
| Clozapine - Food  | 2      | Moderate|
| Paroxetine - Food | 2      | Moderate|
| Atorvastatin - Food| 1     | Moderate|
| Esomeprazole - Food| 1     | Moderate|
| Budesonide - Food | 1      | Moderate|
| Chlorzoxazone - Food| 3     | Moderate|
| Carbamazepine - Food| 1     | Moderate|
| Levocetirizine - Food| 2     | Moderate|
| Theophylline - Food| 1      | Moderate|
| LevoFLOXacin - Food| 1     | Moderate|
| Tamsulosin - Food | 1      | Moderate|
| Fexofenadine - Food| 1     | Moderate|
| Loratadine - Food | 6      | Minor  |
| Caffeine - Food   | 2      | Minor  |
4. CONCLUSION

Drug interactions with other drugs or with foods are common. These interactions could have a beneficial or a harmful effect. Physicians and pharmacists should use programs that detect the drug interactions and to counsel patients about these interactions and also pharmacists should check for drug interactions before dispensing the prescriptions. Moreover, it is important to take the drug two hours after or one hour before eating in order to avoid the harmful effects of these interactions.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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