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Identification of Metronidazole – Drug Interactions at the Outpatient Setting in Alkharj

Nehad J. Ahmad[1*]

[1]Department of Clinical Pharmacy, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Alkharj, Saudi Arabia.

Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

Introduction: Metronidazole is an antibacterial, antiprotozoal and amebicidal agent. It has a good activity against pathogenic anaerobic bacteria, low cost, minor adverse effects and a favorable pharmacodynamic and pharmacokinetic properties but still it interacts with many drugs.
Objective: This study aims to assess the interactions of metronidazole with other drugs at the outpatient setting in Alkharj.
Methodology: This is a retrospective study include revision of the electronic records in the outpatient setting in a public hospital in Alkharj in order to determine the incidence of interactions between metronidazole and other drugs in 2017.
Results: In the present study, the concurrent use of metronidazole with azithromycin, ciprofloxacin, domperidone, formoterol and olanzapine may result in increased risk of QT-interval prolongation and arrhythmias. The use of metronidazole with warfarin may result in increased risk of bleeding.
Conclusion: To dispense and prescribe it appropriately antimicrobial stewardship program should be implemented and checking practice should be implemented to avoid the occurrence of Drug - drug interactions.

Keywords: Adverse reaction; antibiotics; drug interactions; metronidazole.

**Corresponding author: E-mail: pharmdnehadjaser@yahoo.com;*

1. INTRODUCTION

Pharmacovigilance aims to identify and quantify the risks that are associated with the medications use, thus contributing to better understand the main characteristics of adverse drug reactions and the involved mechanisms [1]. These adverse drug reactions represent a common medical problem and can lead to an increased patients' hospitalizations [2,3].

Drug-drug interactions are a common cause of adverse drug reactions; these interactions are common in patients who received several medications such as elderly [4-7]. Poly-therapy increases the risk of drug interactions and can result in the development of ADRs and lead to a reduction or an increase of the clinical efficacy [8-11].

Metronidazole is an antibacterial, antiprotozoal and amebicidal agent [12-15]. It is considered to be a cost-effective drug because of its good activity against pathogenic anaerobic bacteria, low cost, minor adverse effects and a favorable pharmacodynamic and pharmacokinetic properties [16]. But still it interacts with many drugs.

These interactions could be contraindicated such as the interaction with sparfloxacin, major such as the interaction with azithromycin, moderate such as the interaction with ergotamine or minor such as the interaction with phenobarbital. It also interacts with food and is commonly associated with disulfiram-like reactions, this is a major interaction [17,18].

It is important to check and to report adverse drug reactions such as drug – drug interactions in order to prescribe and dispense metronidazole appropriately and also it is important to educate patients how to prevent and manage these adverse drug reactions. So, this study aims to assess the interactions of metronidazole with other drugs at the outpatient setting in Alkharj

2. METHODOLOGY

This is a retrospective study include revision of the electronic records in the outpatient setting in a public hospital in Alkharj in order to determine the incidence of interactions between metronidazole and other drugs in 2017.

The inclusion criteria include the prescriptions that include metronidazole and at least 1 other medication and the exclusion criteria include the prescriptions that don't include metronidazole and the prescriptions that include only metronidazole. All of the topical dosage forms were deleted from the prescriptions.

Data were presented as a percentages and frequencies. Micromedex was used to check for the drug - drug interactions in the prescriptions [19]. Using Micromedex, the interactions were classified according to the severity of an interaction to contraindicated, major, moderate and minor interactions.

3. RESULTS

Between 01-07-2017 till 31-12-2017 there were 123 outpatient prescriptions contained combination between metronidazole and other medications. The most common combination was between metronidazole and paracetamol (28.46%). The medications that were combined with metronidazole are shown in Table 1.

There were no interactions in about 84.55% of the prescriptions. Table 2 shows the severity of interactions.

About 57.89 % of the major interactions were caused by metronidazole interaction with ciprofloxacin. Table 3 shows the interactions between metronidazole and other medications.

4. DISCUSSION

The majority of Metronidazole interactions are either contraindicated or major. Metronidazole interact moderately with acenocoumarol, anisindione, carbamazepine, cholestyramine, cimetidine, cyclosporine, dicumarol, dihydroergotamine, ergoloid mesylates, ergonovine, ergotamine, lithium, lixisenatide, methylergonovine, milk thistle, phenindione, phenprocoumon, phenytoin and silymarin. Moreover, the interaction with phenobarbital is minor. The other interactions are either contraindicated or major [19]. About 57.89 % of the major interactions in the present study were caused by metronidazole interaction with ciprofloxacin, this is rational because metronidazole is commonly prescribed in combination with ciprofloxacin.

In the present study, the concurrent use of metronidazole with azithromycin, ciprofloxacin, domperidone, formoterol and olanzapine may result in increased risk of QT-interval prolongation and arrhythmias. The use of

Table 1. The medications that were combined with metronidazole

Drug	Number	Percentage
Paracetamol	35	28.46 %
Hyoscine-N-Butylbromide	19	15.45 %
Ciprofloxacin	11	8.94 %
Ranitidine	10	8.13 %
Amoxicillin/Clavulanic acid	10	8.13 %
Amoxicillin	7	5.69 %
Omeprazole	5	4.07 %
Metoclopramide	5	4.07 %
Cefuroxime	4	3.25 %
Insulin	4	3.25 %
Metformin	3	2.44 %
Domperidone	3	2.44 %
Aspirin	2	1.63 %
Azithromycin	2	1.63 %
Cotrimoxazole	2	1.63 %
Diclofenac	2	1.63 %
Ibuprofen	2	1.63 %
Paricalcitol	2	1.63 %
Salbutamol	2	1.63 %
Multivitamins	2	1.63 %
Others	27	21.95 %

Table 2. The severity of interactions

Severity of interactions	Number	Percentage
Major interactions	19	15.45%
Moderate interactions	0	0.00%
Minor interactions	0	0.00%
No interaction	104	84.55%

Table 3. The interactions between metronidazole and other medications

The interaction	Number	Severity	Outcome
Metronidazole and azithromycin	2	Major	May result in increased risk of QT-interval prolongation and arrhythmias
Metronidazole and ciprofloxacin	11	Major	May result in increased risk of QT-interval prolongation and arrhythmias
Metronidazole and domperidone	3	Major	May result in increased risk of QT-interval prolongation and arrhythmias
Metronidazole and formoterol	1	Major	May result in increased risk of QT-interval prolongation and arrhythmias
Metronidazole and olanzapine	1	Major	May result in increased risk of QT-interval prolongation and arrhythmias
Metronidazole and warfarin	1	Major	May result in increased risk of bleeding

metronidazole with warfarin may result in increased risk of bleeding. Previous studies stated that some drugs inhibit warfarin's metabolism such as ciprofloxacin, clarithromycin, erythromycin, metronidazole and trimethoprim-sulfamethoxazole and as a result these interactions increase the risk of bleeding [20,21]. Moreover, Ament et al stated that unless the prothrombin International Normalized Ratio can be monitored every other day, medications such as ciprofloxacin, macrolide antibiotics, metronidazole and trimethoprim-sulfamethoxazole in general should not be prescribed to patients who are taking warfarin. Other antimicrobial therapy is recommended for these patients [22].

Additionally, metronidazole interacts with alcohol-containing medications and may cause severe adverse reactions. Alonzo et al reported that the concomitant use of alcohol-containing medications with metronidazole may cause serious adverse reactions and discomfort for the patient. So healthcare providers should watch for symptoms of a disulfiram-like reaction when starting metronidazole or adding concomitant liquid medications to metronidazole therapy [23].

In order to use metronidazole appropriately and to decrease the adverse reactions, antimicrobial stewardship program should be implemented in addition to that it is important to use computerized prescription and decision support systems. Moreover, other interventions that help in choosing the appropriate antimicrobial doses specially if the patient has an impaired kidney function should be implemented [24].

5. CONCLUSION

It can be concluded that metronidazole has a good activity against anaerobic bacteria, it also has low cost, minor adverse effects and a favorable pharmacodynamic and pharmacokinetic properties but still it has a major food drug interaction and also interacts with many drugs that could be serious interactions resulted in increased risk of QT-interval prolongation, arrhythmias and increased risk of bleeding. To dispense and prescribe it appropriately antimicrobial stewardship program should be implemented and checking practice should be implemented to avoid the occurrence of Drug - drug interactions.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The approval of the study by the IRB committee of the ministry of health and after the public hospital approved the study (Log No. 18-474E), the data was collected and after that it was analyzed using Excel software.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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