



The Adverse Effect Reporting for the Most Commonly Used Antibiotics

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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 MIF, DIF and AIF managed the analyses of the study and managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aim: Antibiotics save lives, but the excess use of antibiotics leads to more side effects. Patients benefit from medications but also complain about their adverse effects. This study aims to explore the reports of the adverse effects for the most commonly used antibiotics in Saudi Arabia.

Methodology: The Data regarding the adverse events reports were collected from The National Pharmacovigilance Center in Saudi Arabia. The data include the major allergic reactions and gastrointestinal side effects for the most commonly used antibiotic classes.

Results: The total number of allergic and gastrointestinal adverse effects in 2017 and 2018 for the included antibiotic drugs is 583 reports. The majority of the reports were for penicillin antibiotics (39.96) particularly Amoxicillin/Clavunate.

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Conclusion: The most common adverse effects of antibiotics are allergic and gastrointestinal effects. It is important to report any adverse drug reactions either by health care providers or patients to the Saudi Pharmacovigilance Center.

Keywords: Adverse effect; side effects; reporting; antibiotics; antimicrobial.

1. INTRODUCTION

One of the major principles of clinical practice since the time of Hippocrates is to not harm. Unluckily, adverse drug reactions (ADR) are common in clinical practice despite the efforts of healthcare professionals [1]. All drugs including antibiotics could cause adverse drug reactions. Adverse Drug Reactions include any harmful event that is associated with the usage of a medicinal product [2].

Antibiotics save lives, but the excessive use of antibiotics leads to more side effects and increases the bacterial resistance to antibiotics [3-6]. Tamma et al. [7] reported that about 20% of the hospitalized patients have been shown to develop an adverse reaction related to the use of antibiotics. Furthermore, Shehab et al. [8] reported that approximately 20% of medications associated Emergency Department (ED) visits result from an adverse reaction of one of the antibiotics.

Common side effects are gastrointestinal effects, skin effects such as rash, and thrush; specific effects include the nephrotoxicity and changing the color of the teeth associated with some antibiotic drugs. Therefore, to prescribe an antibiotic by the physicians, the benefits of the antibiotic should outweigh the toxic effects of it. The suitable antimicrobial prescribing should become a priority for all clinicians [9,10].

One of the essential parts of Food and Drug Administration (FDA) systems is the system of post-marketing surveillance and risk assessment programs that aims to identify the adverse events that didn't appear during the drug approval steps. It isn't possible to anticipate all of the side effects of medicine based on pre-approval studies that involve only several hundred or several thousand patients [11,12].

The Saudi Food and Drug Authority (SFDA) was established in 2003. Its objective is to warrant the safety of the drugs and food for both the humans and the animals, and also to ensure the safety of different biological, chemical substances, and electronic products [13]. One of SFDA main

tasks is to establish a suitable regulatory framework to monitor the risk-benefit balance of all registered products throughout their life cycles in the Saudi market [14]. In 2009, the SFDA launched a new pharmacovigilance system that is the Saudi Adverse Event Reporting System (SAERS) to monitor the safety of the post-marketed drugs [15]. The pharmacovigilance system of SFDA receives reports from all regions in Saudi Arabia as well as internationally not only from health care specialists and manufacturers but also from patients [16]. Patients benefit from medications but also complain from their adverse effects, as a result the adverse effects reports that they send should be taken seriously. The leaflet of the drugs should contain an instruction to the patients on how to report ADRs to the national pharmacovigilance centre or to their health providers [17]. This study aims to explore the reports of the adverse effects for the most commonly used antibiotics in Saudi Arabia.

2. METHODOLOGY

This retrospective study includes collecting data regarding the adverse events reports. The data were collected from the National Pharmacovigilance Center in Saudi Food and Drug Authority (SFDA). The data include the major allergic reactions and gastrointestinal side effects for the most commonly used antibiotic classes.

We include allergic reactions such as (skin rash, anaphylactic shock and angioedema) and gastrointestinal side effects (nausea, vomiting, diarrhea and constipation), other side effects were excluded.

We included the following commonly used antibiotic classes:

- Penicillin such as Penicillin G benzathine, amoxicillin, ampicillin.
- Cephalosporin such as cefepime, cefuroxime, cefalexin.
- Macrolide such as azithromycin, erythromycin, clarithromycin.
- Aminoglycoside such as amikacin, gentamicin, tobramycin.

- Fluoroquinolone such as ciprofloxacin, levofloxacin.

The data were collected using excel sheet software and all of the data are presented in the tables by numbers and frequencies.

3. RESULTS

The total number of allergic and gastrointestinal adverse effects in 2017 and 2018 for the included antibiotic drugs is 583 reports. The majority of the reports were for penicillin antibiotics (39.96%) followed by Fluoroquinolones (32.76%). Table 1 represents the number and percentage of adverse effects reports for the most commonly used antibiotic groups.

The majority of the reports were for 2 medications, there were 197 reports for Amoxicillin/clavunate (33.73%) and 162 reports for ciprofloxacin (27.73%). The number and percentage of adverse effects reports for the most commonly used antibiotics are represented in Table 2.

The majority of allergic reactions were for fluoroquinolones (47.17%) followed by penicillin antibiotics (24.43%). On the other side, the majority of gastrointestinal effects were for penicillin antibiotics (63.79%). Table 3 represents the allergic reactions and gastrointestinal adverse effect reporting for the most commonly used antibiotic groups.

4. DISCUSSION

The total number of allergic and gastrointestinal adverse effects in 2017 and 2018 for the included antibiotic drugs is 583 reports. The majority of the reports were for penicillin antibiotics (39.96%) followed by fluoroquinolones (32.76%). The majority of the reports were for amoxicillin/clavunate 197 reports (33.73%) and ciprofloxacin 162 reports (27.73%), followed by cefuroxime 57 reports (9.76%) and azithromycin 52 reports (8.9%).

The majority of allergic effects (mainly rash) were for fluoroquinolones (47.17%) followed by penicillin antibiotics (24.43%) and cephalosporins (14.2%) and this result is rational because rash is common in these antibiotic classes (occur in more than 1% of the patients), but not common in aminoglycosides and macrolides [18]. The allergic reaction reports for fluoroquinolones are more than penicillin antibiotics, this result is in contrast to 2 previous studies which reported that β -Lactams are the most common antibiotic classes reported to cause hypersensitivity reactions [19,20].

CDC reported that about 10% of all U.S. patients report that they had a penicillin antibiotic-associated allergic reaction in their past [21]. But the problem is that rash, for example, can result from other causes not only drugs. Additionally, numerous patients who report that they have penicillin allergies don't have true IgE-mediated reactions and when they evaluated, it is found that fewer than 1% of the population are truly allergic to penicillin antibiotics as reported by the Joint Council of Allergy, Asthma and Immunology and they recommended to identify correctly if the patients are truly penicillin-allergic or no to decrease the excessive usage of broad-spectrum antibiotics [22].

Similarly, the American College of Allergy Asthma and Immunology reported that more than 90% of those who think they have penicillin allergy, really are not. In other words, 90% of the patients who think they are allergic to penicillin are avoiding it without reason [23].

Regarding gastrointestinal effects, the majority of the adverse effects were for penicillin antibiotics (63.79%) followed by fluoroquinolones (13.79%), macrolide antibiotics (12.5%) and cephalosporin antibiotics (9.91%). Broad-spectrum antibiotics exert a more intense effect than narrow-spectrum antibiotics on the gut flora and as a result, cause more diarrhea [24].

Table 1. The number and percentage of adverse effects reports for the most commonly used antibiotic groups

Antibiotic class	Penicillin	Cephalosporin	Aminoglycoside	Fluoroquinolones	Macrolide
Number	233	73	17	191	69
Percentage	39.96	12.52	2.91	32.76	11.83

Table 2. The number and percentage of adverse effects reports for the most commonly used antibiotics

Antibiotic Class	Amikacin	Gentamicin	Tobramycin	Amoxicillin	Amoxicillin, Clavunate	Ampicillin	Penicillin G	Cefalexin	Cefepime	Cefuroxime	Azithromycin	Ciprofloxacin	Levofloxacin	Clarithromycin	Erythromycin
Number	3	13	1	24	197	7	6	2	14	57	52	162	29	15	2
Percentage	0.51	2.22	0.17	4.10	33.73	1.20	1.02	0.34	2.39	9.76	8.90	27.73	4.96	2.56	0.34

Table 3. The allergic reactions and gastrointestinal adverse effect reporting for the most commonly used antibiotic groups

Antibiotic class	Aminoglycoside n (%)	Penicillin n (%)	Cephalosporin n (%)	Fluoroquinolones n (%)	Macrolide n (%)	Total
Allergic reactions	17 (4.82)	86 (24.43)	50 (14.20)	159 (45.17)	40 (11.36)	352
Gastrointestinal effect	0 (0.00)	148 (63.79)	23 (9.91)	32 (13.79)	29 (12.5)	232

The high percentage of reports regarding gastrointestinal effects for penicillin is also rational. The common gastrointestinal adverse effects of amoxicillin and Amoxicillin/Clavunate, include diarrhea, nausea and vomiting occur in more than 1% of the patients. For ampicillin, common gastrointestinal adverse effects include diarrhea. For penicillin G common gastrointestinal adverse effects include nausea and vomiting [18].

For aminoglycosides, there are no reports for the gastrointestinal adverse effects and this is also rational because there are no common adverse effects in the gastrointestinal system for amikacin, gentamicin and tobramycin [18]. But the low number of reports of gastrointestinal side effects for cephalosporin antibiotics is not rational because these antibiotic classes cause several gastrointestinal adverse effects commonly. For example, the common gastrointestinal adverse effects of cephalexin and cefepime include diarrhea. For cefuroxime axetil, common gastrointestinal adverse effects include diarrhea, nausea and vomiting.

Moreover, the low number of reports of gastrointestinal side effects for quinolones and macrolides antibiotic is not rational, because these antibiotics commonly result in gastrointestinal side effects. For example, the common gastrointestinal adverse effects of azithromycin include abdominal pain, diarrhea, flatulence, nausea and vomiting. For clarithromycin, common gastrointestinal adverse effects include abdominal pain, diarrhea, and disorder of taste, indigestion, nausea and vomiting. For erythromycin, common gastrointestinal adverse effects include abdominal pain, diarrhea, and loss of appetite, nausea and vomiting. For ciprofloxacin, the common gastrointestinal adverse effects of include diarrhea, nausea and vomiting. For levofloxacin, common gastrointestinal adverse effects include diarrhea and nausea.

The most common adverse effects of these antibiotic classes are gastrointestinal adverse effect. The low number of reports of gastrointestinal side effects for cephalosporins, quinolones and macrolides may be due to the mildness of these symptoms the majority of these effects are not serious.

The pharmacovigilance specialists should investigate the history of the patients who report

the adverse effects to ensure that the adverse effects are caused by the antibiotics because these adverse effects might be caused by other drugs, some diseases, some foods or by other causes.

5. CONCLUSION

At the end of the study, the usage of antibiotics treats infections but increases the risk of adverse events and if used excessively these medications could lead to the development of bacterial resistance. The most common adverse effects of antibiotics are allergic and gastrointestinal effects. It is important to report any adverse drug reactions either by health care providers or patients to the Pharmacovigilance Center; as a result, it is important to increase the awareness of the public and health care providers on the reporting of adverse effects. Moreover, it is important to take the complete history of the patients to be sure that the adverse effects are caused by the antibiotic not due to other reasons.

CONSENT

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

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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