



RESEARCH ARTICLE

DRUG UTILIZATION REVIEW OF FLUOROQUINOLONES AMONG THE OUT-
PATIENTS IN A PUBLIC SECTOR HOSPITAL, PAKISTAN

Awais Arshaad¹, Shahzaib Sharafat², Ayesha Mustafa^{3*}, Hamza Mahmood⁴, Fatima Mustafa⁵, Sonia Tariq⁶, Ammara Asif⁷

¹Pharmacist, Biogen Life Sciences Distributors, ²Pharmacist, Healthwire online pharmacy, ³Faculty of Pharmacy, Superior University Lahore, ⁴Study coordinator / Pharmacist at Central Park Hospital, ⁵Department of Pharmacy, Superior University Lahore, ⁶Department of Pharmacy, Islamia University Bahawalpur, ⁷Department of Pharmacy, The University of Copenhagen, Denmark.

Corresponding author's email: drayeshamustafa5@gmail.com

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ABSTRACT

Background: The increase in antibiotic resistance is a challenging threat to the healthcare system. Irrational drug use, polypharmacy and the current epidemic of bacterial resistance is attributed to the over use of anti-microbial drugs. **Objectives:** The aim of the current study is to evaluate the utilization pattern of fluoroquinolones, to find significant difference between defined daily dose and prescribed daily dose of such antibiotics. **Methodology:** Quantitative observational, retrospective study was performed to measure the use of antibiotics, specifically Fluoroquinolones in the northern region of Punjab, Gujranwala District, Pakistan. Total 300 patients were enrolled in this study. Data was collected from the patients of all age regardless of their gender, by prescription review. **Results:** Total 300 prescriptions were reviewed to evaluate the prescription pattern of fluoroquinolones in outpatients. Out of 300 prescriptions, the average number of drugs per prescription was 4.5, maximum number of drugs per prescription was 8 and minimum one drug was prescribed in 28 (9.3) prescriptions. The number of prescriptions that contains the drugs without generic names were 71 (23.7) and which contains one drug with generic names were 203 (67.7). Encounter with antibiotic and injection prescribed were 79.3% and 5.3%, respectively. The most commonly prescribed anti-biotic was ciprofloxacin followed by levofloxacin (maximum defined daily dose). **Conclusion:** In this study we observed the drug utilization review of fluoroquinolones antibiotics by evaluating the prescribing patterns among the outpatients. All the study drugs were prescribed by their brand names rather than generic names which is not a rational prescribing and utilization pattern, leading to the enforcement of antibiotic stewardship program.

Keywords: Antibiotic resistance, Defined Daily Dose, Prescribing indicators, Fluoroquinolones.

INTRODUCTION

The rational utilization of medication requires that patients get prescriptions suitable for their treatment, mitigation or prevention of disease, in specific doses that should be according to their own individual needs for a certain period of time, economical to them and their community. There has been a gradual increase in the irrational use of medications and to control it helpful rules were formed by World Health Organization (WHO) during a universal gathering, in 1985 (1).

The trends in the evaluation of the drug use are gradually becoming crucial to encourage rational use of drugs in underdeveloped nations according to the World Health Organization's drug use indicators. An evaluation method can be a survey on prescribing and patient care using drug use indicators from the WHO health center. These quantitative indicators are now widely accepted as a global standard for identifying pitfalls and are used in more than 30 emerging countries (2).

Fluoroquinolones are the broad-spectrum antibiotics. They were introduced as the antibiotic class in 1980. Levofloxacin and ciprofloxacin are most common drugs that are prescribed in Pakistan. The patients having normal functionality of their body function or renal function has the dose of ciprofloxacin 400mg parenterally repeating every 12 hours and the use of oral dose is 500mg repeating after 12 hours. The dose of Levofloxacin is 750 mg orally/IV once daily for 5 days or 500 mg orally/IV once daily for 7-14 days. The purpose of this study is to determine the pattern of antibiotics utilization in the local

hospitals because such antibiotic agents are mostly used in the medication (3).

Drug utilization studies are designed to study the factors with respect to ordering, dispensing and routes of administration of medicine. The frequent use of antibiotics usually causes certain problems such as resistance to that agent, reverse impact on the disease, side effects and increased cost of the treatment, and in order to avoid such circumstances traditional therapy of medicinal plants is recommended (4). Especially fluoroquinolones cause resistance against gram negative strains of infectious bacterium *Escherichia coli*. The increased susceptibility related to infectious microorganisms, diseases of GIT infections and the urinary tract infections in the under-progress countries that have economic problems and have unhealthy environment are increasing day by day. The basic cause of mortality, morbidity and hospital stay is due to long-time non-recovery from microbial infections (5). Activity of microorganisms towards antibiotics after a long period use causes the change in the phenotype relation to susceptibility of microbes. In 2002, many studies described the sufficient time and dose which overcome the bacterial populations phenotype or host that creates the resistance and then we will be successful for treating or terminating the resistant microbes (6).

Antibiotic resistance can cause the serious health related problems and cause the development of severe adverse drug events. The National Antibiotic Use announcements cause reduction in the antibiotic's consumption and ordering, in the China (7). The most common prescribed drugs are ciprofloxacin <CIP>, norfloxacin <NOR> levofloxacin <LEV>. They act by inhibiting bacterial DNA and

stops its growth (8). Resistance is the main effect raised by the use of fluoroquinolones. So, to check the usage of antibiotics pattern, a prospective study was performed in the existing population to get the initial data on drug orders. This study is based on the prescribing indicators given by WHO. Fluoroquinolones are used against the MDR strains of *Mycobacterium tuberculosis*. Fluoroquinolones resistance develops in *mycobacterium* therefore they are used in combination with other anti-TB drugs (9). As antibiotics are used for short period of time and defined daily dose (DDD) do not express the doses used in prescription, so a compact method is used to know the utilization of drugs (10). Our goal is to check the published article ATC/DDD which is the anatomical classification system contains the authentic references (11), the anatomical therapeutic classification (ATC) and defined daily dose (DDD) determination. Due to repeated alternation and creation of association and uses repeated addition of ATC system is necessary, therefore this study will provide an intact assessment of study designs that will complete help to cooperate the setup of the hospital. Analysis of all the anti-microbial drugs used in hospital according to defined daily dose basically tells about the trends of prescribing pattern of antibiotics (12). In this study, the antibiotics are classified according to anatomical classification system. When the administered daily dose is reduced for a patient with impaired renal function, the method of define daily dose will underrate antibiotic exposure. This will be relevant when the ratio of patients suffering from renal impairment in a hospital differs from that in the other hospital. Moreover, define daily dose is

not applicable on the overall antibiotics used by the children, obtained from purchased records. Finally, if there is any difference between the administered daily dosage and WHO approved define daily dose, then methodology will not give a precise estimate of the duration of treatment (13). Drug tolerance in *Mycobacterium tuberculosis* is caused by regular change in the DNA chromosomes that completely relay on drug target. Tolerance of specific drug will occur at the particular rate and extent but medicinal plants being used for the treatment purpose are less prone to cause drug resistance (14).

Study Objectives

The prime significance of study is to provide the information about the use of fluoroquinolones and gradual increase in the dose of antibiotic. The significant data regarding the drug utilization of the antibiotics will be obtained in terms of a devised system at international level in order to overcome the drug resistance problems. In order to reduce the irrelevant use of antibiotics in the hospitals, drug policies and guidelines are followed. Significance of this type of study provides knowledge about how to utilize this type of drugs. It is basically the rate at which the certain fluoroquinolones work, cause the ADRs and resistance. The intention of this survey is to evaluate the antibiotic usage among 300 OPD patients by define daily dose according to Anatomical Therapeutic Classification system. The foremost objective of this study was to describe the pattern of antibiotic consumption in the hospital.

MATERIALS & METHODS

Study Design and Setting

Retrospective study was performed to quantify the drug utilization pattern of antimicrobials, specifically fluoroquinolones in a specific population. Drug utilization research group developed the Anatomical Therapeutic Classification system (ATC) /Define Daily Doses (DDD) system to evaluate, to analyze and to influence the use of drugs (26). The study was carried out in the public sector hospital at northern region of Punjab, Gujranwala District, Pakistan. The hospital has all the basic departments and services, including OPD, pediatric and emergency department. Drug utilization program included all the departments of hospital in which the study drugs were in use, and to identify the patients receiving the studied drug. In order to do that, patient's prescriptions were reviewed. Ethical Approval was obtained from Pharmacy Research Ethics committee (PREC) of The Superior College, Lahore (IRB # 74-P-2018/PREC).

Study Population

The population study was performed on general population of all age groups, who visited the public sector hospital during the study period including both genders receiving the antibiotics for the prophylaxis, treatment or cure of the disease.

Sampling Procedure

The data was collected from patients who received Fluoroquinolones or at least one of the studied drugs, either for prophylaxis or treatment, from THQ Hospital and other public sector Hospitals, Gujranwala. The prescriptions of all the patients who visited the hospital during the study period and

were prescribed at least one antibiotic were reviewed to identify the patients receiving study drugs.

Inclusions Criteria

All prescriptions containing at least one antibiotic being collected during the study period of October to December 2018 are included.

Exclusion Criteria

All the prescriptions not including any antibiotics, and except for the mentioned study period are excluded in this study.

Data Collection and Instrument

The amount of drug used must be calculated in order to enable the comparison in drug utilization studies. In accordance with WHO and DDD methodology, drug consumption is expressed in DDD/1000 inhabitants × day (27). Anatomical Therapeutic Classification system developed by the WHO, assigned a specific defined daily dose (DDD) to every substance used and all the data was collected from the patients of all age regardless of their gender, by prescription review. Data included the drug name, strength and quantity prescribed.

Data Processing and Analysis

To compare the values of prescribed daily dose (PDD) and defined daily dose (DDD) of Fluoroquinolones ATC/DDD index 2018 was used, while Statistical analysis was carried out by SPSS. However, for the comparison of mean Student t-test was used and in order to check out the association between qualitative variables Chi² test was utilized.

RESULTS

We have 300 patients in this study who received fluoroquinolones during the study period. Most of the patients were female,

includes 131 (43.7%) males and 169 (57.3%) females. The mean age of the patients was 31.31 and std. deviation was 17.671. The percentage of males and females is given in the following table 1.

Table 1. Demographic description.

Gender	No. of participants	Percentage
Male	131	43.7%
Female	169	57.3%
	Mean	Std. deviation
Age	31.31	17.671

The utilization of fluoroquinolones antibiotics was evaluated by using WHO prescribed indicators. The first prescribing indicator was about to check the number of drugs per encounter or to check the number of drugs prescribed with fluoroquinolones. Minimum one drug prescribed to 28 (9.3%) patients while maximum eight drugs prescribed to 1 (3.0%) patient. The frequencies and percentages of the number of drugs from 2-7 are given in the Table 2.

The second prescribing indicator was related to check the number of drugs prescribed by generic. All the prescriptions were reviewed to check the number of drugs prescribed by generic names and 71 (23.7%) prescriptions were without any drug prescribed by generic, while maximum 4 drugs were prescribed by generic in 1 (0.3%) prescription as given in the Table 2. The third prescribing indicator was encounter with antibiotic prescribed. During our study period minimum one antibiotic was prescribed in 238 (79.3%) prescriptions, two antibiotics were in 61 (20.3%), while maximum three

antibiotics were prescribed in 1 (0.3%) prescription as given in the table 2.

The fourth prescribing indicator was about the number of prescriptions containing injections. Out of 300 prescriptions 284 (94.7%) were without any injection while 16 (5.3%) prescriptions contained one injection as given in the table 2. Last prescribing indicator was to check the number of drugs prescribed from the essential drug list. According to our data record in 300 prescriptions all the drugs that prescribed were present in essential drug list 2018.

Table 2. Prescribing indicators

Prescribing indicators	No. of antibiotics per prescription	Frequency (%)
No. of drug per encounter	1	28 (9.3)
	2	25 (8.3)
	3	55 (18.3)
	4	83 (27.7)
	5	65 (21.7)
	6	35 (11.7)
	7	8 (2.7)
	8	1 (3)
Drug prescribed by generic	0	71 (23.7)
	1	203 (67.7)
	2	18 (6.0)
	3	7 (2.3)
Encounter with antibiotic prescribed	4	1 (0.3)
	1	238 (79.3)
	2	61 (20.3)
	3	1 (0.3)
Encounter with injection prescribed	0	284 (94.7)
	1	16 (5.3)
Drug prescribed from essential drug list	1	300 (100)

The comparison of define daily dose and prescribed daily dose is given in the table 3. The prescribed daily dose was obtained from the prescriptions while define daily dose was calculated by using WHO collaborating center for drug statistics methodology, ATC/DDD index. ATC code for ciprofloxacin is J01MA02 and its defined daily dose according to ATC/DDD index was 1g and it was prescribed as 500mg two times a day. ATC code for levofloxacin is J01MA12 and its DDD was 0.5g while it was prescribed as 500mg two times a day as seen in table 3 below.

Table 3. Comparison of DDD & PDD

ATC code	Drugs	DDD	PDD	Route of administration	Units
J01MA02	Ciprofloxacin	1	1	O	g
J01MA12	Levofloxacin	0.5	1	O, I/V	g

DISCUSSION

In this retrospective study, we observed the DUR of fluoroquinolone antibiotics. We enrolled total 300 patients and review their prescriptions to evaluate the prescribing patterns and utilization of fluoroquinolones among the outpatients. All the study drugs were prescribed by their brand names rather than generic names and mostly economical brands were used. In our study the most commonly used drug was Ciprofloxacin and then was the prevalence of use of Levofloxacin. However, in the United States the trend

was contrary and usage of former was higher than the latter (28).

In another study that was conducted in Belgium, Ciprofloxacin was the most commonly prescribed Fluoroquinolones, illustrating 253 prescriptions (96.6%), while other prescribed study drugs that were prescribed in that study were moxifloxacin (1.1%), followed by norfloxacin (0.4%), and levofloxacin (1.9%) (29). During the period, 20 patients of age 15 years or less were subjects of research on safety and efficacy of ciprofloxacin in children in underdeveloped countries was reviewed by Green S et al, and they stated that Ciprofloxacin along with other medicinal plants are safe and efficacious (30, 33).

According to our study, ciprofloxacin is found to be most frequently prescribed drug. A same study was performed in America in which fluoroquinolones were prescribed in sinusitis and skin infections (1). In an Indian study, DDD/100 bed days for FQ's were 33.5%. It indicates highest percentage of ciprofloxacin (15.72%) followed by levofloxacin (12.54%). The highest percentage of prescribed drug was also ciprofloxacin in our study (22). The use of fluoroquinolones rose by three-folds in United States between 1995-2002. This increase was due to activity of FQ's against *S. pneumoniae* 42% of fluoroquinolones were prescribed to the patients who had unapproved diagnosis (31).

In the United States, in 2002, it is estimated that patients younger than 18 years, like children and infants approximately 520000 prescriptions for fluoroquinolones were written. Clinical trials of fluoroquinolones in pediatrics cause arthrotoxicity, musculoskeletal events, CNS disorders, prolongation of QT

interval, disorders of glucose homeostasis, hepatic dysfunction, photosensitivity, rashes and multi-drug resistance (32). There are several infectious diseases along with their comorbidities which need to be cured by antibiotics, such infections are also treated by using medicinal plants based on the therapeutic effects of antimicrobial phytoconstituents present in them (34,35). The traditional use of medicinal plants not only ensures cost effectiveness but also improves the quality of life of patients (36).

CONCLUSION

Polypharmacy, prescribing the brand, irrational prescribing of antibiotics, improper consultation time and patient burden are the major key elements that ultimately causing resistance against antibiotics. The most widely prescribed FQs recommended the intake of Ciprofloxacin trailed by Levofloxacin. We have observed that usage of quinolones was higher than those revealed in past investigations though the parenteral FQ use was lesser than those reported in past examinations. This is not a bad sign as the injectables are costly, need of expert person and likewise there is risk of transmission of infections. We recommend that there is a need of rules and arrangements in regards to the utilization of FQs. This will adequately limit the errors on the utilization of antibiotics which may ultimately lead to rational medication use and better consideration on patients.

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DECLARATIONS

Authors' Contributions

AA contributed to study concept; SS and AM contributed to study design, data collection. AA and HM contributed in data analysis and interpretation. FM did the literature review and critically reviewed the manuscript. All the authors read and approved the final manuscript.

Ethical Approval

Ethical Approval was obtained from Pharmacy Research Ethics committee (PREC) of The Superior College, Lahore (IRB # 74-P-2018/PREC).

Conflict of Interest

The author declared no conflict of interest among them.

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