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Research Article

Drug utilization review of ciprofloxacin in the outpatient department of Boru Meda Hospital, South Wollo Zone, Amhara Region, Ethiopia

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ABSTRACT

Background: The antimicrobial agents developed during the last 60 years are among the most dramatic examples of the advances of modern medicine. Many infectious diseases once considered incurable and lethal are now amenable to treatment with a few pills. They are among the most frequently prescribed medications to day although microbial resistance due to evolutionary and misuse threatens their continued efficacy. One mechanism to ensure correct prescribing and use is drug use evaluations studies. Objective of current study is to evaluate retrospectively of ciprofloxacin use from outpatient medical records by using pre- set criteria in Boru Meda hospital.

Methods: A cross-sectional study on retrospectively collected data was used to evaluate ciprofloxacin use from outpatient medical history records existing from January 18, 2009 to January 17, 2010. Criteria along with thresholds set by experts for undertaking drug use evaluation for ciprofloxacin was used which is modified based on Ethiopian National Drug Formulary and Ethiopian National Standard Treatment Guideline, which are used in the hospital. Data was collected from January 18 to January 25, 2010 using appropriate data collection format.

Results: Twenty six (65%) patients were in the age group of 15 to 49 years and twenty (50%) were females. Thirty eight (95%) and each of thirty seven (92.5%) cases were consistent with the Ethiopian National Standard Treatment Guideline & drug formulary regarding indication, dose & frequency of ciprofloxacin use in the outpatient department of Boru Meda hospital. 47.5% ciprofloxacin use has problem in duration of treatment . There were potential drug interactions with the drug in 40% of the cases. 10% of ciprofloxacin use was against contraindication.

Conclusions: Due From the retrospective Drug Use Evaluation (DUE) study, it was identified that there was inappropriate ciprofloxacin use in the outpatient department of Boru Meda hospital even though the drug's use regarding indications was a better performance and dosing practices were almost appropriate as per the criteria used for the study (assuming that there were no dose adjustments). There was a great problem concerning the duration of ciprofloxacin drug therapy. Ciprofloxacin use along with potentially interacting drugs and against contraindications was also another problem indicated in the study.

Keywords: Drug use evaluation, BMH, STG, Ciprofloxacin, Boru Meda

INTRODUCTION

Antibiotics are microbial metabolites or synthetic analogs inspired by them that, in small doses, inhibit the growth and survival of microorganisms without serious toxicity to the host. Empirical therapy, definitive therapy, and prophylactic or preventive therapy are possible with these agents. Many infectious diseases once considered incurable and lethal are now amenable to treatment with a few pills. Antibiotics are among the most frequently prescribed medications today although microbial resistance due to evolutionary pressures and misuse

threatens their continued efficacy. Unfortunately we cannot any longer confidently depend upon the discovery of an increasing numbers of novel antibiotics and antimicrobial agents to keep infectious diseases under control but must increasingly pay attention to neglected public health measures and concentrate upon using antibiotics safely and effectively.[1-3]

One of the most pressing problems facing public health providers and administrators in many countries is ensuring rational use of drugs. The conference of Experts on the Rational Use of Drugs, convened by the World Health Organization (WHO) in Nairobi in 1985 defined rational drug use as "the rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time and at the lowest cost to them and their community.[4]

Rational drug use implies an individual approach to patient treatment .The presence of standard treatment guidelines and drug formularies for selected drugs in a health facility does not ensure that they are prescribed and used correctly. One mechanism to ensure correct prescribing and use is drug use evaluation (DUE).[4]

DUE is a performance improvement method that focuses on evaluating and improving drug use processes to achieve optimal patient outcomes. DUE may be applied to a drug or therapeutic class, or diagnosis. Through its focus on the system of drug use, DUE helps to identify actual and potential drug -drug related problems that could interfere with achieving optimum outcomes from drug therapy. DUE is of three types; prospective, concurrent and retrospective.[5,6]

A retrospective DUE is the simplest to perform since drugs therapy is reviewed after patient has received the medication. A retrospective review may detect patterns in prescribing, dispensing or administering drugs to prevent recurrence of inappropriate use and serves as a means for developing prospective standards and target interventions. In retrospective DUE, patient medical charts or computerized records are screened to determine whether the drug therapy met approved criteria and aids prescribers in improving care for their patients, individually and within groups of patients.[6]

Quinolones are groups of antimicrobial drugs having a wide clinical application. The introduction of fluoroquinolones such as ciprofloxacin represents a particularly important therapeutic advance because these agents have broad antimicrobial activity and are effective after oral administration for the treatment of a wide variety of infectious diseases. Antimicrobial prophylaxis often with an oral fluoroquinolones is used to prevent a variety of infections in patients undergoing organ transplantation or receiving cancer chemotherapy.[2]

Ciprofloxacin, being second generation fluoroquinolones, has wide clinical importance. It is the most frequently used fluoroquinolone in the United States and also included in the National Drug List of Ethiopia to be used for a variety of bacterial infections. It has paramount importance in treating infections caused by many *Enterobacteriaceae* and other gram negative bacilli. Ciprofloxacin is the most potent of fluoroquinolones for pseudomonal infections associated with cystic fibrosis. It is the drug of choice for prophylaxis and treatment of anthrax.[7,8]

Statement of the problem

Although antimicrobial drugs are among the safest and least toxic of drugs used in medical practice, they are also included under the most commonly misused of all drugs. Excessive amounts can result in significant toxicities especially in patients with impaired drug excretion or metabolism. The use of too low a dose may result in treatment failure and is most likely to select for microbial resistance. Hence dosing errors which can be the wrong frequency of administration or the use of either an excessive or sub-therapeutic dose are common in using antimicrobial agents.[2]

The development of bacterial resistance of antibiotics has become a major problem throughout the world. Resistant organisms may emerge as a result of many factors, including irrational use of drugs one form of which is irrational prescribing practice. Studies have shown that 22-65% of antibiotic prescriptions are inappropriate.[9-11]

An inevitable consequence of antimicrobial usage is the selection of resistant microorganisms. Overuse & inappropriate use of antibiotics has fueled a major increase in prevalence of multidrug resistant pathogens, leading some to speculate that we are nearing the end of the antibiotic era.[3]

Fluoroquinolones are extremely useful agents and an important therapeutic advance. They are relatively nontoxic, well tolerated, broad spectrum agents. Their excellent oral bioavailability permits their use for treatment of variety of serious bacterial infections such as those caused by *Pseudomonas aeruginosa* or Methicillin Resistant *Staphylococcus aureus* (MRSA), which formerly could be treated only with parental agents. As strains of *E .coli* and other gram negative pathogens resistant to trimethoprim-sulfamethoxazole have become more common, fluoroquinolones are increasingly relied on for empirical therapy of urinary tract infections.[3]

Unfortunately overuse and inappropriate use have already eroded the clinical utility of fluoroquinolones. Overuse of the fluoroquinolones particularly in the hospital settings, has led to selection of resistance and this resistance has increased after their introduction into clinical practice especially in *Pseudomonas* and *Staphylococci*.[2,3]

Studies on ciprofloxacin in different places showed that; in 2004 the prevalence of ciprofloxacin resistance was 7% in Cape Town and 11% in Johannesburg. In 2007, 37/139 (27%) Cape Town isolates, 47/149 (32%) Johannesburg isolates were resistant to ciprofloxacin in comparison with 2004 data; this represents 2-9 fold and 1.9 fold increase respectively. These increases, in part, associated with over use of ciprofloxacin.[12]

Significance of the study

The study design to evaluate the use of ciprofloxacin in Boru Meda hospital to provide an over view ciprofloxacin use in hospital and to promote the rational prescribing, dispensing, and administration of ciprofloxacin. Hence to reduce the emergence of antibiotic resistance. More over the study contributes in identifying medication related problems and areas of in appropriate use by that it helps in identifying areas in which further information and education may be needed by health care providers.

Furthermore, the study helps for policy makers, baseline for other studies, guides other health care providers to prescribe drugs correctly.

General Objective

To evaluate retrospectively of ciprofloxacin use from outpatient medical records by using   pre-set criteria in Boru Meda hospital

Specific Objectives

- To evaluate whether ciprofloxacin is appropriately indicated or not
- To evaluate whether the dosage regimen (dose, frequency, duration) is in accordance with guidelines used in the hospital
- To assess any drug -drug interactions with concomitantly administered drugs
- To assess extent of contraindications

METHODS

Study area and period

The study was conducted in Boru Meda hospital which is found in south wollo zone, Amhara region. It is located 410 kms far from Addis Ababa and only 10 kilometers from Dessie town which is the center of the zone. There are 3 private & 3 governmental hospitals in south wollo zone, Boru Meda hospital being one of the governmental hospitals. There are 42 health professionals working in the hospital: 1 specialist, 3 general practitioners & 2 pharmacists among others. The study was conducted from January 18 to January 25, 2010.

Study Design

A cross sectional, retrospective study was done to evaluate ciprofloxacin use using a pre -set criteria along with threshold which was set based on the National STG & formulary used in the hospital. Patient medical history cards existing from January 18, 2009 to January 17, 2010 was evaluated against the pre-set criteria using appropriate data collection format.

Population

Source population

All the patient medical history cards in Boru Meda hospital during the period of January 18, 2009 to January 17, 2010.

Study population

All medical history cards of outpatients containing ciprofloxacin in Boru Meda hospital during the period of January 18, 2009 to January 17, 2010.

Sample population

The sample population was determined depending on drug use evaluation guideline.

Sample size

The size of the sample population was determined according to the Joint Commission on the Accreditation of Health care Organization (JCAHO) criteria which mandates a sample size of: 5% If the average number of cases per quarter is greater than 600 and at least 30 , if quarter cases are less than 600. From the study which encompasses 1 year data of ciprofloxacin use in the outpatient department of Boru Meda hospital, the number of cases (ciprofloxacin indications) per quarter was found to be 204(a total of 815 annual cases). Therefore 40 was the size of sample in the study.[19]

Sampling technique

40 outpatient medical history cards were selected using systematic random sampling method from sequentially arranged cards (by date of ciprofloxacin indication) of outpatients that were on ciprofloxacin (Cfx) in the hospital during the period of January 18, 2009 to January 17, 2010. Every 20th card was taken as a sample population (sampling interval=total source population/sample size=>815/40=20).

Study variables

Independent variables

- Patient characteristics: age, sex, pregnancy, lactation
- Diagnosis: qualification of prescribers

Dependent variables

- Indication
- Dosage regimen (dose, frequency, duration)
- Drug-drug interaction
- Contraindication

Data quality control

Data collection format containing the variables to be measured was developed and used. Maximum care was taken for the quality of the data to be collected.

Data Collection

Obtaining permission to conduct the study, the data was collected using a pre-tested data collection format by the principal investigator.

Data processing and Analysis

The collected data was manually sorted, categorized and then results were evaluated against the set criteria and thresholds, and presented in tables.

Pre- test

The data collection format was pre-tested for its validity, reliability and consistency.

Ethical consideration

Prior to data collection, formal letter was written from Jimma University Student Research Program to Boru Meda hospital so as to conduct the study.

Limitation of the study

Unavailability of adequate literature on the subject matter of the study & poor patient medical history taking practice (especially drug history) were worth mentioning as limitations to prepare this research paper.

RESULTS

Age and sex distribution of patients with ciprofloxacin indication

A total of 40 outpatient medical history cards indicated with ciprofloxacin were included in the study. Out of 40 patients, 20 (50%) were males and 20 (50%) were females who were neither pregnant nor lactating. 3, 26 and 11 of the patients were in the age ranges of < 15 years, 15-49 years and > 50 years respectively (Table 1).

Indications of ciprofloxacin

Ciprofloxacin was indicated for a variety of disease conditions. 85% of ciprofloxacin used was indicated for the treatment of Acute Gastro Enteritis (AGE, 30%), Urinary Tract Infections (UTIs, 30%), Acute Febrile Illnesses (AFIs, 15%) and bacterial conjunctivitis (10%) (Figure 1).

Table 1: Age and sex distribution of patients with ciprofloxacin indication in the outpatient department of Boru Meda hospital, January 18, 2009 to January 17, 2010.

Variable	Frequency (%)
Age (Years)	
<15	3 (7.5)
15-49	26 (65)
>50	51 (27.5)
Total	40 (100)
Sex	
Male	20 (50)
Female	20 (50)
Total	40 (100)

Indication Appropriateness of ciprofloxacin

Thirty eight (95%) ciprofloxacin indications were appropriate based on Ethiopian National Drug Formulary (2004 edition) used in the hospital. Only 2(5%) indications were not in line with the formulary which was indications for varicose vein and intestinal parasite infections.

Dosage regimen (dose, frequency, duration) of ciprofloxacin

It was found that out of 40 outpatient medical history cards, 37 (92.5%) contained correct ciprofloxacin dosing while 3 (7.5%) cards contained over dosing. There were no under dosing regimens. 37 (92.5%) indications were with correct frequency of administration while 3 (7.5%) with incorrect frequency. 21 (52.5%), 18 (45%) and 1 (2.5%) cards contained correct, long and short duration of treatment respectively (Table 2).

Drug interactions with ciprofloxacin

Forty percent (16) of cards contained one or more potentially interacting drug with ciprofloxacin. Paracetamol, diclofenac, and antacids accounted 7 (17.5%0, 7 (17.5%) and 2(5%) of the interacting drugs respectively.

Ciprofloxacin use against contraindications

There were no pregnant and lactating patients for whom ciprofloxacin was indicated in the study, but it was indicated for four (10%) children whose ages were <18 years which is against contraindications.
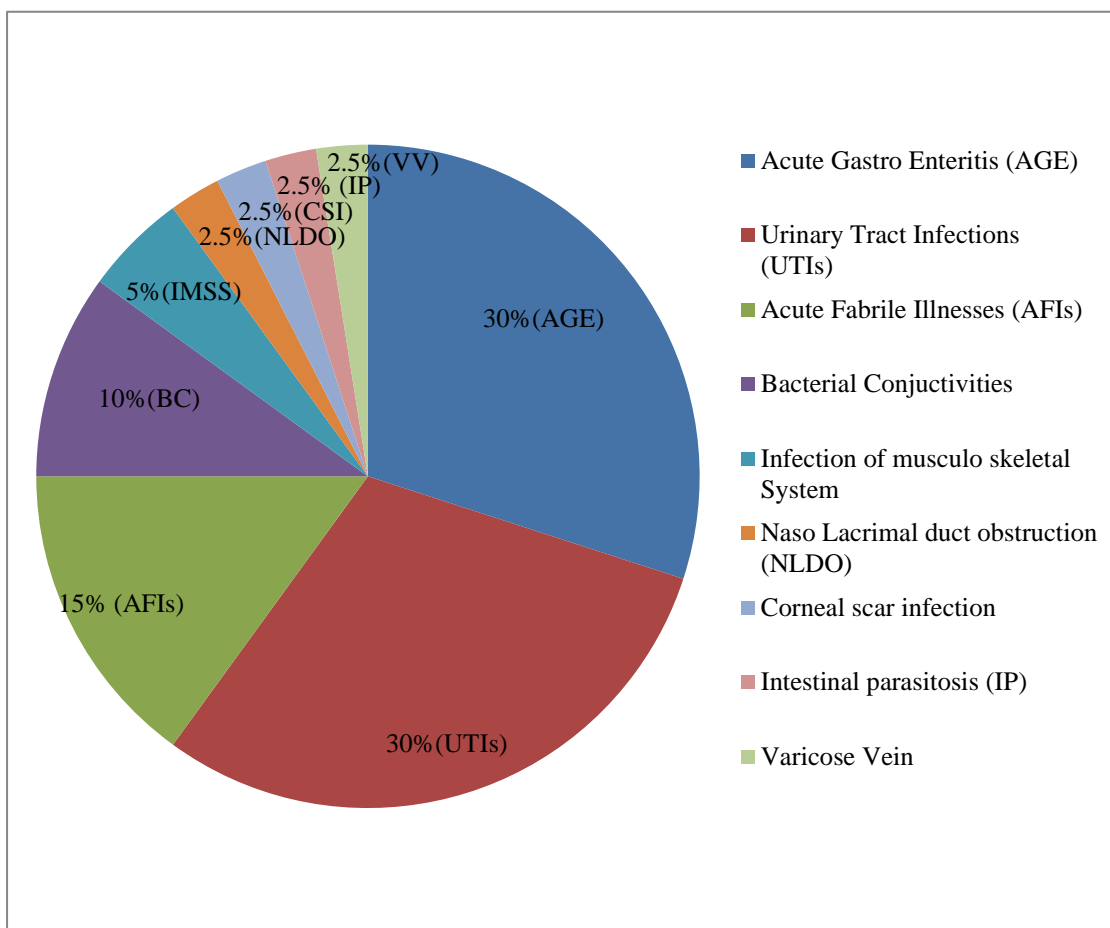
Figure 1: Disease conditions for using ciprofloxacin in the outpatient department of BMH, January 18, 2009 to January 17, 2010.

Table 2: Dosage regimen (dose, frequency, duration) of ciprofloxacin in the outpatient department of Boru Meda hospital, January 18, 2009 to January 17, 2010.

Indicators	Variable	Frequency (%)	Sex		Age (years)		
			Male	Female	<15	15-49	>50
Dose	Correct dose	37 (92.5)	19	18	3	24	10
	Under dose	-	-	-	-	-	-
	Over dose	3 (7.5)	1	2	-	2	1
	Total	40 (100)	20	20		2	1
Frequency	Correct frequency	37 (92.5)	19	18	3	23	11
	Incorrect frequency	3(7.5)	1	2	-	3	-
	Total	40 (100)	20	20	3	26	11
Duration	Correct duration	21 (52.5)	12	9	3	11	7
	Short duration	1 (2.5)	-	1	-	1	-
	Long duration	18 (45)	8	10	-	14	4
	Total	40 (100)	20	20	3	26	11

Actual performance versus set criteria & thresholds for ciprofloxacin

From the study, it was found that 95% of ciprofloxacin indications were appropriate, 92.5% and 52.5 % of indications contained correct doing and duration of the drug respectively, and 60% of the cards were free from potential drug interactions while 90% of ciprofloxacin use was not against contraindications (Table 3).

Table 3: Actual performance versus set criteria and thresholds for ciprofloxacin in the outpatient department of Boru Meda Hospital, January 18, 2009 to January 17, 2010.

Criteria	Expectation / Threshold No (%)	Actual performance No (%)
Indication	36(90)	38(95)
Dose	38(95)	37(92.5)
Duration	38(95)	21(52.5)
Drug interaction	36(90)	24(60)
Contraindication	40(100)	36(90)

DISCUSSION

Diabetes The purpose of Drug Use Evaluation is to ensure that drugs are used appropriately, safely and effectively to improve patient health status. In addition, continual improvement in the appropriate and effective use of drugs has the potential to lower the overall cost of care.[6]

Success of treatment largely depends on the ability of a physician to diagnose the major health problems (s) of a patient, select the correct drug, dosage form and route of administration, foresee probable adverse reactions and drug interactions, and prevent unnecessary or dangerous duplication of therapy. Implementation of hospital drug formulary can be considered the basis of rational drug use. However the existence of a rationally derived list of drugs approved for procurement and use in a hospital does not ensure that they are prescribed and used correctly.[4]

Drugs have to be prescribed (indicated) appropriately, on the basis of clinical diseases identified through diagnosis. Hence, prescribers should stick with standard treatment guidelines (STGs) while prescribing any drug. Regarding to the indications of ciprofloxacin, the study showed that 95% of the indications were appropriate as per the national drug formulary which is even a better performance as compared with the threshold set for indication of ciprofloxacin (90%). The result is almost similar to a retrospective study done in Cleveland, veterans Administration Medical Center, which revealed that 100% ciprofloxacin uses were appropriate.[14]

Different doses of ciprofloxacin are used for a variety of infections and age groups. Sub clinical use of the drug results in ineffective control of infectious diseases while overdose results in toxicity problems. Therefore optimal dose has to be used for optimal treatment out comes. 92.5% correct dose & 7.5% overdose practices were revealed in the study (assuming that there were no dose adjustments). There were no under dosing of ciprofloxacin identified. This is more than the percentage revealed from a retrospective study conducted in Central North Carolina , in 10 community nursing facilities which showed that, out of 95 regimens ,only 81% ciprofloxacin dosing were correct. 19% regimens contained inappropriate dosing of which 5.7 % regimens with potentially suboptimal dosing (under dose) while 13.3% doing were over the appropriate (optimal) dose (over dose).[13]

Drug resistance has become a great problem associated with the use of antimicrobial agents. Prolonged use of ciprofloxacin, one of the antimicrobial agents can lead to emergence of microbial drug resistance. Hence it should be used appropriately according to the duration of treatment needed with the particular disease available in STGs and formularies. Inappropriate duration of therapy was the major problem revealed by the study in the study hospital. Only 52.5 % ciprofloxacin uses were with correct duration of therapy which is very far from the threshold set for ciprofloxacin duration of therapy (95%) . 2.5% of the indications were with short treatment periods while long treatment periods accounted for 45% of indications which can lead to development of resistance . This result showed less percentage of correct duration as compared with a retrospective study done in central North Carolina which revealed only 8% excessive (long) duration of therapy.[3,13]

The simultaneous use of two or more drugs is recommended in specifically defined situations based on pharmacological rational. However, selection of an appropriate combination requires an understanding of the potential for interaction between the drugs. Interactions may, otherwise, affect the patient negatively, from the study; it was found that 40% of ciprofloxacin use had one or more potentially interacting drug of which paracetamol & diclofenac (Analgesics) each accounted 43.75% and antacids 12.5% of the interacting drugs. Co-administration of ciprofloxacin with analgesics may cause convulsion. Absorption of the drug may be interfered with antacid containing Al or Mg. Drug interaction results are different from the threshold set for drug interaction with ciprofloxacin (90%). This difference might be due to the practice of prescribing multiple drugs together.[2]

Prescribing drugs against contraindications should be avoided unless the benefit of doing so outweighs the risk. Ciprofloxacin was used despite contraindications in 10% of the cases, children under 18 years old. The pregnancy and lactation history of female patients who were in the fertile age group (60%) and history of patients with known hypersensitivity reaction to ciprofloxacin and other quinolones were not documented. This might imply that the drug may have been used in such type of patients for whom ciprofloxacin use is a contraindication practice. The result is different from the threshold set for contraindication use with ciprofloxacin which mandates 0% use against contraindications (a threshold value of 100%).

To date, there are no published studies conducted on retrospective DUE of ciprofloxacin in Ethiopia, hence it was not possible to compare the practice of Boru Meda

hospital with practices of other clinical settings in Ethiopia. Also due to unavailability of adequate relevant literature to the topic , the findings were discussed mainly in relation to ciprofloxacin use criteria cited in the 2004 national drug formulary and national STG of Ethiopia which were found in the hospital to guide safe , effective and appropriate drug therapy .

CONCLUSION

From the retrospective Drug Use Evaluation study, it was identified that there was inappropriate ciprofloxacin use in the outpatient department of Boru Meda Hospital even though the drug's use regarding indications was a better performance and dosing practices were almost appropriate as per the criteria used for the study(assuming that there were no dose adjustments). There was a great problem concerning the duration of ciprofloxacin drug therapy. Ciprofloxacin use along with potentially interacting drugs and against contraindications was also another problem indicated in the study.

Recommendations

- If the gains from appropriate drug therapy are needed to be maximized, prescribers should stick with standard treatment guidelines while prescribing drugs
- Regular Drug Use Evaluation studies have to be undertaken in clinical settings where multiple drugs are prescribed so that appropriate, safe & cost effective drug therapy can be given to patients.
- It is important for health facilities to arrange trainings on rational prescribing practice to prescribers.

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Acronyms and Abbreviations

BID- Twice a day
BMH- Boru Meda Hospital
CFX- Ciprofloxacin
DUE- Drug Use Evaluation
DUR- Drug Use Review
GI- Gastro Intestinal
HIV/AIDS- Human Immuno Deficiency Virus / Acquired Immuno Deficiency Syndrome
IV- Intra Venous
MRSA- Methicillin Resistant Staphylococcus Aureus
OPD- Out Patient Department
PI- Principal Investigator
RTIs- Respiratory Tract Infections
STG- Standard Treatment Guideline
UTIs- Urinary Tract Infections
VAMCC- Veterans Administration Medical Center, Cleveland
WHO- World Health Organization

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