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DRUG USE EVALUATION OF CEFTRIAXONE: THE CASE OF AYDER REFERRAL HOSPITAL, MEKELLE, ETHIOPIA

Firehiwot Amare Abebe [1], Derbew Fikadu Berhe*[1], Abera Hadgu Berhe [1], Hailemichael Zeru Hishe [1] and Melaku Asfawuwessen Akaleweld [2]

Department of Pharmacy [1], Department of Medicine [2], College of Health Sciences, Mekelle University, Mekelle-Ethiopia

ABSTRACT

Assessment of antimicrobial use can be performed by evaluating their use. Drug use evaluation is a performance improvement method that focuses on evaluation and improvement of drug use processes to achieve optimal patient outcomes. The objective of this study was to evaluate the rational use of ceftriaxone in Ayder referral Hospital, Mekelle-Ethiopia. Retrospective cross sectional study was used to assess rational use of ceftriaxone. The study was conducted by reviewing medication records of 296 patients who received ceftriaxone during hospitalization at Ayder referral Hospital from September 11, 2009 to September 10, 2010. A systematic sampling method was used to select inpatient prescriptions with ceftriaxone and patient cards were located based on the medical record number on the prescription papers. Data was collected by using structured format and evaluated against WHO criteria for drug use evaluation as per standard treatment guideline of Ethiopia. Most patients were dosed as 2 g/day (79.4%). The duration of therapy was found to be high in the range 2-7 days (51.69%). Ceftriaxone was mainly used as preoperative prophylaxis (38.8%). Maintenance fluids were the most commonly co-administered medications with a frequency of 62.16%. The use of ceftriaxone was appropriate only in 106 cases (35.8%) for the justification of use. Most of inappropriate uses were seen in terms of duration. Consistency of prescriber to the national standard treatment guideline was found to be low. To improve rational use and prevent the development of resistance; prescribers should adhere to the national standard treatment guideline. Intensification of short term trainings and antibiotic control systems are some of the possible solutions the hospital has to do.

INTRODUCTION: In developing countries, infectious diseases are the most common causes of morbidity and mortality [1]. Antibiotics represent approximately 30% of acute care hospitals drug expenditure and are prescribed for 20-50% of inpatient [2]. Use of antibiotics has contributed to the dramatic fall in morbidity and mortality from communicable and infectious disease over the last 50 years globally [1]. However, the control of infectious disease is seriously threatened by the steady increase in the number of microorganisms that are resistant to antimicrobial agents [3]. Emergence of antimicrobial resistance is a result of the use, over use and misuse of antibiotics [1].

The increased prevalence of known resistant organisms and the emergence of newly resistant organisms have resulted in delays in effective therapy and the length of hospitalization and have led to increased costs for patients. When considering this, the logical first step is to evaluate the suitability of antibiotic usage. Antibiotic use evaluation is a basic measure for evaluating the appropriate usage of antimicrobial agents [4].

Drug use evaluation (DUE) is a system of ongoing, systematic criteria based evaluation of drug use that will help ensure that medicines are used appropriately at the individual patient level [5, 6, 7]. DUE may be applied to a drug, therapeutic class, disease state or condition, a drug use process or outcomes [6]. DUE can assess the actual process of medication prescribing, administration, or dispensing. It involves a comprehensive review of patients' prescription and medication data before, during and after dispensing in order to assure appropriate therapeutic decision-making and positive outcome [7]. If properly developed, it not only provides a means of identifying drug use problems but also provides a means to correct the problem and there by contribute to rational drug therapy [8].

DUE performed in in-patient settings to identify trends of use and appropriateness of prescribing pattern and survey have shown that 22-65% antibiotic prescriptions are either inappropriate or incorrect [1, 9]. When considering this, targeting antibiotics that are prescribed frequently for drug use evaluation would be important to extend the useful life of the antimicrobial agents [10].

Cephalosporins are the most widely used antibiotics for treating common infections [3]. The cephalosporins are a large group of related β-lactam antimicrobial agents with broad spectrum of activity, low rates of toxicity and ease of administration. Various cephalosporins are effective for treatment of many conditions, including pneumonia, skin and soft tissue infections, bacteremia and meningitis [11]. Cephalosporins are classified by "generation"; first, second, third and fourth. In general, lower-generation cephalosporins have more gram-positive activity and higher-generation cephalosporins more gram-negative activity [12].

Due to their activity against most gram-negative organisms and their availability, third generation cephalosporins are most commonly used. Among third generation cephalosporins, ceftriaxone is the most commonly prescribed drug [13].

Ceftriaxone is one of the most commonly used antibiotics due to its high anti bacterial potency, wide spectrum of activity and low potential for toxicity [4]. It is used to treats different types of bacterial infections including bronchitis, pneumonia, bone infections, abdominal and skin infections, urinary tract infections and others. Despite its wide spectrum use, there are trends showing the misuse of ceftriaxone. This study is designed to evaluate the use of the drug at Ayder Referral Hospital.

Objective: This study was conducted to evaluate the use and appropriateness of ceftriaxone in different wards of Ayder Referral Hospital, North Ethiopia and attempted to compile basic data outlining the appropriate use of the antibiotic.

METHODOLOGY:

Study setting: The study was conducted from July 2011- September 2011 in Ayder Referral Hospital (ARH) located in Mekelle, capital city of Tigray regional sate, North Ethiopia. ARH is teaching Hospital of Mekelle University and the only Referral Hospital in Tigray Regional State.

Study Design: The criteria used for antibiotic selection in this study were antibiotic with a risk of abuse, antibiotic with high consumption rate, drug that was not being controlled by antibiotic prescribing restriction system. Accordingly, Ceftriaxone a broad-spectrum parenteral cephalosporin was selected. A retrospective cross sectional study was conducted on 296 patient cards selected using systematic random sampling method from in-patient prescriptions with ceftriaxone. Data was collected from patients' medication records who receive ceftriaxone during hospitalization in Ayder referral Hospital from September 11, 2009 to September 10, 2010. The data was collected from patient cards using structured data collection format and then the result was evaluated against the standard treatment guideline of Ethiopia for General Hospital.

Data Collection: Data collection format was developed according to WHO recommendation and validated to our context. It was pretested on thirty patients' cards and the necessary changes made. Each case from the patient medication records was evaluated against the STG of Ethiopia for indication, dosage, frequency and duration of ceftriaxone therapy.

Statistical Analysis: The data was processed and analyzed by using WHO criteria for drug use evaluation as per standard treatment guideline of Ethiopia. Four WHO criteria namely indication for use, dosage, frequency and duration were used to evaluate ceftriaxone use.

Ethical Consideration: The study was approved by Mekelle University, College of Health Sciences Research and Ethics committee. Permission letter was then secured from Medical director office of Ayder Referral Hospital. The confidentiality of data collected was maintained. Name and address of patient and prescriber was omitted from the data collection format.

RESULTS: A total of 296 patient cards out of 336 were found to have complete information for the intended purpose of ceftriaxone. Among the 296 patients, 138(46.6%) were female and 158(53.4%) male. The average age of the patients was 34.3 (ranging 1 day to 83 years). Most of them were adults being in the range 14-65(73.31%) (**Table 1**). In 235(79.4%) cases, ceftriaxone was dosed as 2g/day (**Table 2**).

TABLE 1: AGE AND SEX DISTRIBUTION OF PATIENTS INCLUDED IN THE STUDY

Age (years)	Frequency		Sex	Frequency	
	#	%		#	%
< 14	49	16.55	Male	138	46.62
14-65	217	73.31			
>65	30	10.14	Female	158	53.38
Total	296	100		296	100

Age distribution was biological classification (pediatrics, adults and geriatrics)

TABLE 2: CEFTRIAXONE DAILY DOSING DISTRIBUTION

Daily dosage (gm/day)	<2	2	2-4	4
Frequency	49(16.6%)	235(79.4)	235(79.4)	11(3.7%)

The mean duration of ceftriaxone use was 7.2 days (ranging 1 day to 32 days) (**Table 3**).

TABLE 3: DURATION OF CEFTRIAXONE THERAPY DISTRIBUTION

Duration (days)	No of patients	Percent
Stat	5	1.69
1 day	31	10.47
2-7 days	153	51.69
8-14days	83	28.04
15-21days	15	5.07
>21 days	9	3.04

Among the 296 cases, 190(64.2%) were found to be inappropriate (not according to the Ethiopian STG). While the rest 106(35.8%) were appropriate (**figure 1**).
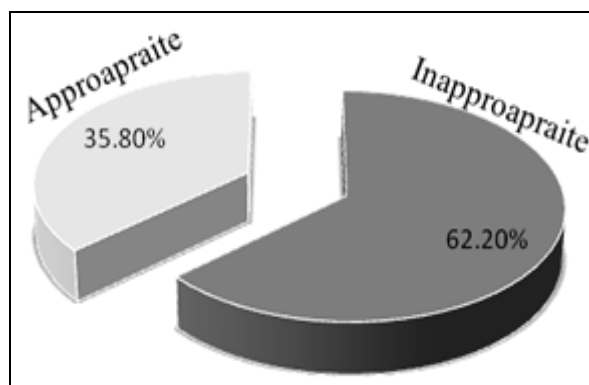
FIG. 1: APPROPRIATENESS OF CEFTRIAXONE UTILIZATION IN ARH AGAINST THE STG AND WHO SET CRITERIA

Most cases of ceftriaxone utilization was involved in surgical ward 108(36.5%); the remaining were in internal medicine (medical ward) 100(33.8%); pediatrics ward 45(15.2%); ICU and emergency ward 24(8.1%) and gynecology and obstetrics ward 19(6.4%). The highest inappropriate use (in percent) was from pediatrics ward 38 of 45(84.4%) followed by; gynecology and obstetrics 14 of 19 (73.7%); ICU and emergency 16 of 24 (66.7%); surgery 69 of 108 (63.8%) and internal medicine 53 of 100 (53%) (**Figure 2**).
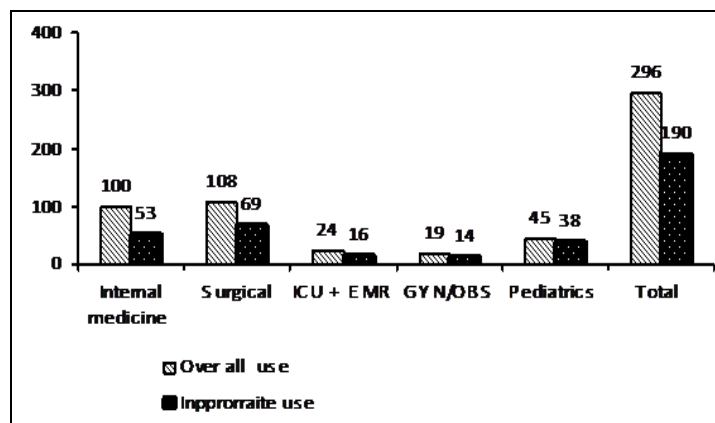
FIG. 2: OVER ALL AND INAPPROPRIATE USE OF CEFTRIAXONE IN DIFFERENT WARDS OF ARH

Among the drugs co-administered with ceftriaxone, maintenance fluids were the most commonly used (62.16%) (**Table 4**).

The most common indication of ceftriaxone was preoperative prophylaxis followed by pneumonia, sepsis, urinary tract infection, typhoid fever and others (**Table 5**).

TABLE 4: FREQUENTLY CO-ADMINISTERED DRUGS WITH CEFTRIAXONE

Drug	Frequency (Number)	Frequency (Percent)
Maintenance fluid	184	62.16
Diclofenac	113	38.18
Metronidazole	91	30.74
Anti TB	42	14.19
Furosemide	39	13.18
Pethidine	37	12.50
Paracetamol	32	10.81
Cimetidine	30	10.14
Cloxacilin	30	10.14
Metocloperamide	25	8.45

TABLE 5: THE MOST COMMON DISEASES FOR WHICH CEFTRIAXONE WAS PRESCRIBED

Assessment	Appropriate	Total no.	Percentage	Inappropriate	Percentage
Peri operative prophylaxis	115	34	29.57	81	70.43
Pneumonia	63	22	34.92	41	65.08
Sepsis	62	20	32.26	42	67.714
UTI	29	15	51.72	14	48.28
Meningitis	14	5	35.71	14	64.29
Typhoid fever	8	6	75	2	25
Others	4	1	25	3	7

DISCUSSIONS: In our study, the use of ceftriaxone was found to be appropriate for the justification of use in 106 cases (35.8%) (Figure 1) which is lower than the value obtained in a retrospective evaluation conducted in Black lion hospital, Addis Ababa (71.43%) and Police Hospital, Addis Ababa (73.02%) [14]. This difference might be attributed to the fact that Black Lion Hospital and Police Hospital are well experienced and equipped with sufficient professionals. In fact, Ayder Referral Hospital is only with 5 years of experience.

The appropriate use of ceftriaxone obtained in this study is also lower than that obtained in a prospective use evaluation of ceftriaxone conducted in 10 Hospitals of Korea (65.5%) [4]. This difference may be attributed to the fact that the study conducted in Korea was prospective, evaluation of a patient's drug therapy before medication is dispensed, and consider patient outcome, which can be mentioned as one of the drawback of our study (retrospective study).

Additionally, the study in Korea used a number of criteria like culture and sensitivity test and other laboratory results, which are lacking in patient medical record of Ayder referral hospital. The appropriate use of ceftriaxone in our study (35.8%) is close to the result obtained in Port of Spain, Trinidad (38%) [13].

The use of ceftriaxone was found to be high in surgery ward (36.5%) followed by, Internal medicine (33.8%), pediatrics (15.2%), ICU & Emergency (8.2%) and gynecology (6.4%). This pattern is similar in trend obtained in Port of Spain, Trinidad, high in Surgery (61.48%), and followed by Internal medicine (13%) [13]. Most of the inappropriate uses involved in Pediatrics ward (84.4%) (Figure 2). The high percent of inappropriate use in pediatrics ward may account to the fact that diseases are complicated in the age group and adjustment of dose and duration might have been needed.

The mean duration of ceftriaxone therapy was found to be 7.2 days and high in the range 2-7 days (51.69%) followed by 8-14 days (28.04%) which is lower than that obtained in Korea 10.3 days [4]. This is an important factor as the number of days in which an antibiotic is used correlates with resistance prevalence [15].

Additionally, this may indicate the prevalence of diseases in which ceftriaxone was used in the range mentioned above. The most frequent indication for ceftriaxone use was preoperative prophylaxis (38.85%) unlike that obtained in Port of Spain, respiratory tract infection [13].

Despite not being recommended for surgical prophylaxis in Ethiopian STG, ceftriaxone use is indicated in different product information. The STG recommended the use of 750 mg cefazolin by IV 30-45 min before incision and 2nd dose if operation takes more than 3 hrs in preoperative prophylaxis. However, considering the indication for use of ceftriaxone its use has not been questioned in the study [16]. The second most frequent indication was pneumonia (21.28%) followed by sepsis (20.94%), urinary tract infection (UTI) (9.8%), meningitis (4.73%) and typhoid fever (2.7%).

Among the medications co-administered with ceftriaxone, maintenance fluids take the first place with frequency of (62.16%) followed by diclofenac (38.18%), metronidazole (30.74%) and Anti TB drug (14.19%). This shows the co-morbid condition of bacterial disease with diseases for which the medications are indicated. Ceftriaxone was co-administered with ringer lactate in 98 cases (33.1%) which is lower than that obtained in Black lion Hospital, Addis Ababa (40.9%) and Police Hospital, Addis Ababa (44.4%) [14]. This increases the probability of IV incompatibility of ceftriaxone with calcium containing drugs, which includes ringer lactate [9]. This indicates the presence of medication related problem namely IV incompatibility with respect to ceftriaxone use.

CONCLUSIONS AND RECOMMENDATION: Drug use evaluation of ceftriaxone with respect to indication, duration of therapy, and frequency of administration shows the of the prescription practice. In Mekelle University Ayder Referral Hospital, as to WHO set criteria, prescribers were not sticking to Ethiopian National STG. The majority of inappropriateness was seen with duration of therapy.

Result of the study showed that inappropriate use of ceftriaxone is high which paves a way for the emergence of bacterial strains that are resistant to the available antimicrobial agents, which in turn leads to increase in cost of therapy and treatment failure. Hence, we recommend the following;

1) Setting antibiotic control system

2) Intensification of educational and training programs

3) Easy access of the national STG to all Health professionals and;

4) Setting continuous drug use evaluation program.

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