

Drug Use Evaluation of Ceftriaxone in Medical Ward of Mizan Aman General Hospital, Bench Maji Zone, South Western Ethiopia

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Abstract

Background: Third generation cephalosporin are most commonly used cephalosporin, ceftriaxone being the most commonly prescribed. It is used to treat different types of bacterial infections. To assure efficacy and safety of drugs, they have to be prescribed and dispensed rationally. Drug use evaluation is a performance improvement of drug use processes to achieve optimal patient outcomes. The study aimed to evaluate the utilization of ceftriaxone in medical ward of Mizan Aman general hospital.

Materials and Methods: A retrospective cross sectional study was conducted from March 15th, 2012 to March 15th, 2015. Medication records of 403 patients who were admitted and prescribed ceftriaxone during the previous three years to the study period were evaluated against the Ethiopian Standard Treatment Guidelines (2014) as a reference. Patient cards were selected using systematic random sampling technique. Data was collected by using structured data abstraction format.

Results: The majority of patients were female 218 (54.1%). The most frequent age group was adults in the range 25-34 y (35.8%). COPD, PUD and Bronchial Asthma were the most common co-morbid diseases which accounts for 9.2%, 6.9% and 5.7% respectively. Ceftriaxone was mainly used for the treatment of pneumonia (46.2%). Chest X-ray was the most commonly used evidence for the diagnosis. The use of ceftriaxone was appropriate only in 158 cases (39.2%). Most of inappropriate uses were seen in terms of duration of therapy (81.9%) followed by inappropriate dose (12.3%) and frequency (5.8%).

Conclusion: From this study it was observed that the most common indication of ceftriaxone was Pneumonia, followed by Meningitis. Most of the patients were improved and discharged from the hospital. Four to seven days were the most frequent hospital stay. The study also showed that there is high inappropriate use of ceftriaxone. The majority of inappropriateness was seen with duration of therapy.

Keywords: Ceftriaxone; Evaluation; Medical; Mizan-Aman

Abbreviations: AFI: Acute Febrile Illness; AGE: Acute Gastro-Enteritis; BID: Twice per day; CBC: Complete Blood Count; COPD: Chronic Obstructive Pulmonary Disease; CSF: Cerebro Spinal Fluid; CV: Cardiovascular; DTC: Drug Therapeutic Committee; ESR: Erythrocyte Sedimentation Rate; FHRH: Felege Hiwot Referral Hospital; HTN: Hypertension; LAMA : Long acting Muscarinic Antagonists; MAGH: Mizan Aman General Hospital; NSAID: Non-Steroidal Anti-Inflammatory Drugs; PUD: Peptic Ulcer Disease; RVI: Retro Viral Infection; STG: Standard Treatment Guideline; TASH: Tikur Anbessa Specialized Hospital; UTI: Urinary Tract Infection

Introduction

Infectious diseases are the most common cause of morbidity and mortality in developing countries and various classes of antibiotics are frequently used to prevention as well as treatment. Antibiotics are among the most common medications prescribed both in the hospital setting and the community setting. The overuse of antibiotics has resulted in the emergence of drug-resistant strains which are very difficult to treat, representing major public health problem. Antibiotics represent approximately 30% of acute care in hospitals and they are prescribed for 20%-50% of patients in medical ward [1].

In addition to overuse, extended duration of use of suboptimal concentrations and longer hospital stay are additional risk factors that have contributed to the emergence of antimicrobial resistance that cause considerable impact on patient treatment and outcomes adding to the increased length of stay in the hospital, additional co-morbid condition

and increased treatment cost. When considering this, the logical first step is to evaluate the appropriateness of antibiotic usage. Antibiotic use evaluation is a basic measure for evaluating the appropriate usage of antimicrobial agents [2]. Irrational use of antibiotics can have several problems, such as increase in side effects and treatment costs for both patients and health care system. Since antibiotics are one of the major prescribed drugs for hospitalized patients, studying the rational use in this class of drugs can be very valuable [3].

Cephalosporines are the most widely used antibiotics for treating common infections. These are a large group of β -lactam related antimicrobial agents with broad spectrum of activity, low rates of toxicity and ease of administration. Various cephalosporines are effective for treatment of many conditions, including pneumonia, skin and soft tissue infections, bacteremia and meningitis. They are

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classified by generation; first, second, third and fourth. In general lower generation cephalosporines have more gram positive activity and higher generation have more gram negative activity. Due to their activity against most gram negative organisms and their availability, third generation cephalosporines are the most commonly used generation. Among third generation cephalosporines, ceftriaxone is the most frequently prescribed drug [4,5]. It is used to treat different types of bacterial infections, including bronchitis, pneumonia, bone infections, abdominal and skin infections, urinary tract infections and etc. [6].

The major causes of inappropriate use of ceftriaxone are lack of the knowledge of physicians, nurses and other health professionals on pharmacology and pathophysiology, lack of skill in diagnosis and attitude towards selecting the most appropriate and cost effective treatment. This might lead to emergence of antimicrobial resistance and adverse drug reaction [7]. The other consequence of inappropriate use of ceftriaxone is delay in effective therapy and length of hospitalization [8].

In the world, annual cost of infection caused by antibiotic resistant bacteria is estimated to be \$4-5\$ million due to inappropriate use [9]. This problem has been recorded in Africa. In Ethiopia the use of broad spectrum antibiotics, in particular the third generation cephalosporines in nosocomial infection have been linked to the emergence of antibiotic resistance, length of hospitalization and increase in cost [10]. As general, the more frequently antibiotic is used, the higher the rate of emergence of bacterial resistance. A study which has been done in Ayder referral hospital, Mekelle, Ethiopia, shows that the appropriate use of ceftriaxone was only 35.8% and the rest was inappropriate [11].

Although there are some studies done in different parts of the country, there is no research conducted in the study area on ceftriaxone use evaluation among hospitalized patients. In order to fill this gap, this study was aimed to conduct the drug use evaluation of ceftriaxone in medical ward of MAGH.

Methods

Study area and period

The study was conducted in Mizan Aman General Hospital (MAGH) located in Mizan-Aman town which is 561 kilometres far from the capital city of Ethiopia, Addis Ababa. It is the only general hospital for Bench Maji Zone. It gives both inpatient and outpatient services. The hospital has different units such as internal medicine, pediatrics, Gynecology/Obstetrics, surgical ward, and hospital pharmacy with 171 health professionals. The study was conducted from March 15th, 2012 to March 15th, 2015 in Mizan Aman General Hospital.

Study design

A retrospective cross-sectional study design was employed.

Source population

All charts of patients admitted to medical ward of MAGH.

Target population

All charts of patients admitted to and prescribed ceftriaxone in medical ward of MAGH from March 15th, 2012 to March 15th, 2015.

Study population

Complete medication records of patients who received ceftriaxone during hospitalization at medical ward of Mizan Aman General Hospital from March 15th, 2012 to March 15th, 2015.

Inclusion and exclusion criteria

Inclusion criteria

- Patients admitted to medical ward and who were prescribed ceftriaxone.
- Age greater than or equal to 15 years old.

Exclusion criteria

- Patient's record with insufficient information.
- Records of patient from wards other than medical ward.

Sample size determination

Sample size was determined by using the formula:

$$n = z^2 p (1-p) / d^2$$

Where: n is minimum size, Z is the reliability coefficient at 95% confidence interval, *i.e.* 1.96; p is proportion of population possessing the characteristics of interest. p was taken as 50% to calculate the minimum sample size; there is no similar study done in or around the study area. d is precision or margin of error as 5%.

$$n = (1.96)^2 \times 0.5 (1-0.5) / (0.05)^2 = 384$$

To compensate for incomplete patient cards, by adding contingency of 5% = 384 × 5% = 19, the actual sample size was obtained to be: n = 384 + 19 = 403.

Study variables

Independent variables

- Age
- Sex
- Diagnosis
- Co morbidities
- Co medication

Dependent variable

- Ceftriaxone use

Sampling techniques

The study used stratified random sampling technique. Records collected in three years were considered as one main stratum and divided into three strata based on the year the data was recorded. Each stratum was divided into twelve sub strata by considering records collected in all twelve months of the year which gives thirty six total number of sub strata. From each sub stratum 11 or 12 patient cards were randomly selected.

Data collection instrument

The data was collected by using structured data abstraction format and drug use evaluation was performed by reviewing patient medication records. Data collection format that comprises patient information such as age, indication, and drug information like dose, frequency, and duration of administration was used to collect data.

Data collectors

The data was collected by two trained data collectors under supervision of the investigators.

Data processing and analysis

The data was processed and analyzed manually by using tallying method and scientific calculator.

Ethical consideration

The ethical clearance was obtained from department of pharmacy, Mizan Tepi University and support letter was delivered to Mizan Aman General Hospital. Permission was secured from the hospital before conducting the data collection.

Result

Socio-demographic characteristics

Among 403 patients, more than half (56.3%) were female and the most frequently encountered age groups were between 25-34 (35.73%) followed by 15-24 (21.58%) (Table 1).

The indications of ceftriaxone

Even though almost half (43.9%) of the study subjects had co morbidities, only the disease for which ceftriaxone prescribed was taken as a major indication while the remaining were recognized as co morbidity. The most common indication for which ceftriaxone prescribed was Pneumonia (46.15%) followed by Meningitis (21.8%) and UTI (15.9%) while osteomyelitis and variceal hemorrhage were indications for which ceftriaxone was prescribed rarely (Table 2).

Co-morbid diseases

Co morbidity, in addition to major indication, has been seen in 177(44%) of the study subjects. Among this, subjects found with more than one co morbidities account for 28(7%) and total number of co morbidity was 205. COPD was the most (22.6%) frequently observed co morbidity and followed by PUD (19.2%) and bronchial asthma (13.5%) (Table 3).

Evidence for infection

Almost all (93.1%) indications were evidenced. Most of major indications were confirmed by chest X-ray (27.1%) and followed by CSF

Age (years)	Males (N=176)	Percent (%)	Females (N=227)	Percent (%)	Total (N=403)	Percent (%)
15-24	37	21	50	22	87	21.6
25-34	68	38.6	76	33.5	144	35.7
35-44	23	13.1	51	22.5	74	18.4
45-54	32	18.2	32	14.1	64	15.9
55-64	5	2.8	9	4	14	3.5
65 and above	11	6.3	9	4	20	5
Total	176	43.7	227	56.3	403	100

Table 1: Age and sex distribution of patients included in the study at MAGH.

Indications	Number of cases, N=403	Percent (%)
Pneumonia	186	46.2
Meningitis	88	21.8
UTI	64	15.9
AGE	28	6.9
Cellulites	9	2.2
Septic arthritis	9	2.2
AFI	9	2.2
Variceal hemorrhage	5	1.2
Osteomyelitis	5	1.2

Table 2: The indications of ceftriaxone at MAGH.

Co-morbid diseases	Frequency	Percent (%)
COPD	40	19.5
PUD	34	16.6
Bronchial asthma	24	11.7
RVI	18	8.8
Malaria	14	6.8
HTN	13	6.3
Complicated measles	9	4.4
Adult malnutrition	9	4.4
Hypovolemic shock	6	2.9
Anasarca	5	2.4
Dysentery	9	4.4
Intractable vomiting	6	2.9
Variceal hemorrhage	7	3.4
Chronic diarrhea	11	5.4
Diagnosis without co-morbid	226	56
Total	205	50.8

Table 3: Co-morbid diseases in the study at MAGH.

(20.6) and ESR (16.9). Ultrasound was the most rarely used evidence for diagnosis (Table 4).

Co-administered drugs

Corticosteroids were the most (40.2%) frequently co-administered medications while cardiovascular medications were rarely (2.2%) co-administered (Table 5).

Hospital stay (in days)

The majority (60.8%) of patients were hospitalized in medical ward for a period of 4-7 days, followed by 28.8% for 8-14 days and 6.9% for 1-3 days (Figure 1).

The appropriateness of ceftriaxone use

Inappropriate use of ceftriaxone has been seen in more than half 245 (60.8%) of the cases while the remaining 158 (39.2%) were appropriate (Figure 2).

Distribution of inappropriate use of ceftriaxone

Among inappropriate use of ceftriaxone, majority, 201 (82%), of cases were in terms of the duration of treatment followed by in terms of dose 30 (12.2%) and in terms of its frequency 14 (5.7%) (Figure 3).

Ceftriaxone dosing at MAGH, March 15, 2012-March 15, 2015

Mostly, ceftriaxone was given as 1 gm BID among 296 (73.4%) whereas it was 2 gm BID in the remaining, 107 (26.6%), cases (Figure 4).

Duration of ceftriaxone therapy

About 83.9% of ceftriaxone regimens were given for the period of 2-7 days, followed by 13.6% for 8-14 days (Figure 5).

Clinical outcome of ceftriaxone therapy

Greater than three-fourth, 320 (79.4%), of subjects were improved at the end of treatment. While 65 (16.1%) subjects were died, only four cases were referred to higher health facility (Figure 6).

Discussion

In this study ceftriaxone utilization was classified as appropriate

Diagnosis with evidence	Frequency (n=375)	Percent (93.05%)
Chest X-ray	109	27.1
CSF	83	20.6
ESR	68	16.9
Urinalysis	60	14.9
AFB	14	3.5
Blood film	16	4
CBC	18	4.5
Ultrasound	7	1.7
Diagnosis without evidence	Frequency (n=28)	Percent (7)
Total	403	100

Table 4: Evidence for diagnosis for which ceftriaxone is prescribed in the study at MAGH.

Drugs	Frequency (n)	Percent (%)
NSAIDs	134	33.3
Acid suppressants	42	10.4
Corticosteroids	162	40.2
Antimicrobials	75	18.6
C.V drugs	9	2.2
Respiratory medication	46	11.4
Others	149	37

Table 5: Frequently co-administered drugs with ceftriaxone at MAGH.

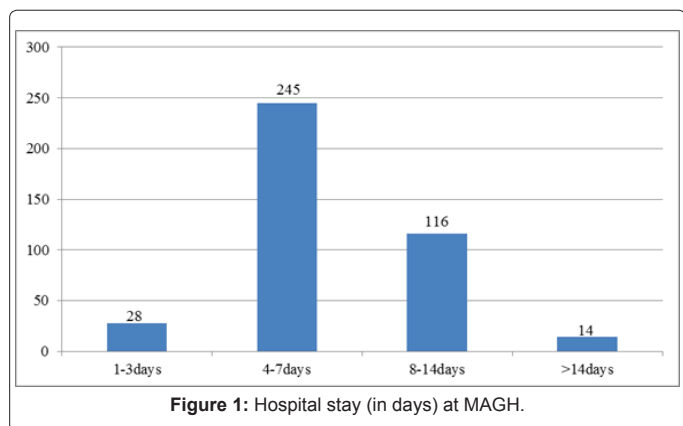


Figure 1: Hospital stay (in days) at MAGH.

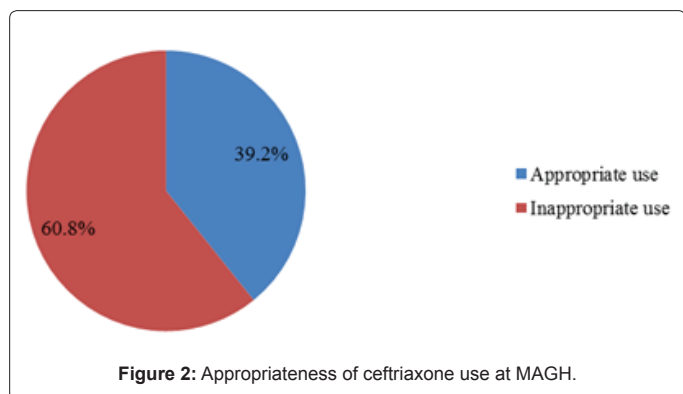


Figure 2: Appropriateness of ceftriaxone use at MAGH.

and inappropriate by using Ethiopian Standard Treatment Guideline, 2014 as a reference. Indications, dose, frequency, and duration of the treatment were evaluated against the STG for their appropriateness. Almost half (44%) of the study subjects were found with co morbidity and COPD was the most (19.5%) frequently observed one.

The use of ceftriaxone was found to be high for the treatment of pneumonia (46.2%) followed by meningitis (21.8%). This pattern

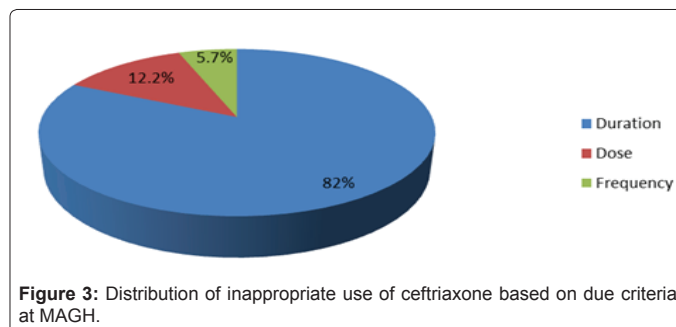


Figure 3: Distribution of inappropriate use of ceftriaxone based on due criteria at MAGH.

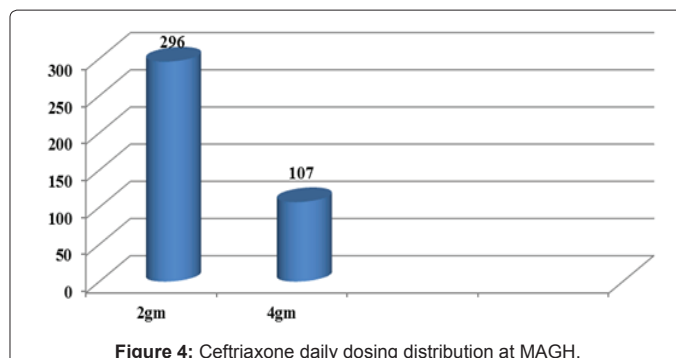


Figure 4: Ceftriaxone daily dosing distribution at MAGH.

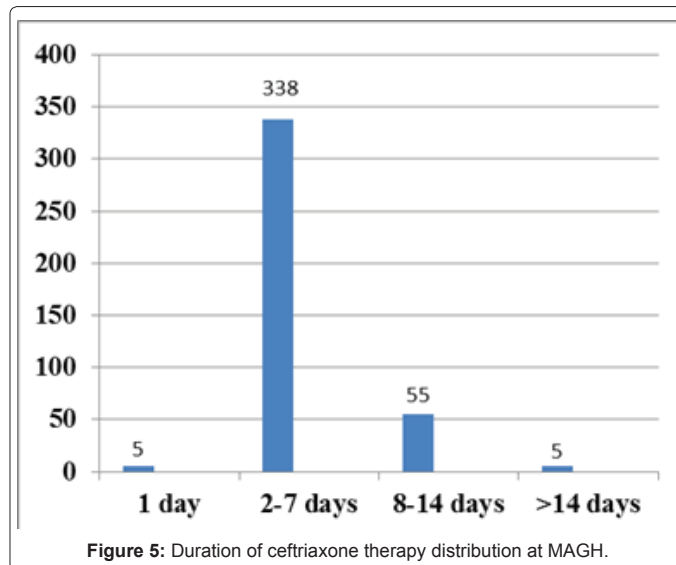
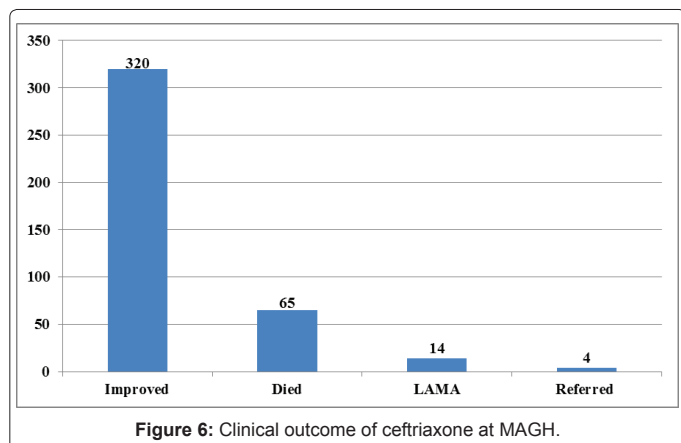


Figure 5: Duration of ceftriaxone therapy distribution at MAGH.

was not similar in trend obtained in Port of Spain, Trinidad, high for respiratory tract infection (52.2%) and followed by UTI (39%) [6]. But in Ayder referral hospital, Mekelle, Ethiopia preoperative prophylaxis followed by pneumonia(21.28%), sepsis (20.9%), urinary tract infection (UTI) (9.8%), meningitis (4.7%) and typhoid fever (2.7%) [11] and in Dessie referral hospital pneumonia (49.1%) followed By meningitis (30.4%), Urinary tract infection (20.9%), sepsis (4.3%), AGE (3.8%), STI (1.3%), Typhoid fever (1%) and dyspepsia (0.6%) [12]. This difference may be attributed to variable distribution of the infectious diseases due to geographical area, socio-economic and sanitation differences or it may be due to inconsistent prescription of ceftriaxone and poor adherence to standard treatment guidelines among health professionals in different hospitals.

In this study, the use of ceftriaxone was found to be appropriate among 158 cases (39.2%), which is lower than the value obtained in a



retrospective evaluation conducted in Dessie referral hospital, Dessie (53.8%), Tikur Anbessa Specialized Hospital (TASH), Addis Ababa (71.4%), Police Hospital, Addis Ababa (73%), and 10 Hospitals of Korea (65.5%), [12-14,8], respectively. This difference might be attributed to the fact that Dessie referral Hospital, TASH, Police Hospital and Ayder referral hospital are well experienced and equipped with sufficient professionals and controlling agents like Drug therapeutic committee (DTC) when compared with the MAGH Hospital but higher than Ayder referral hospital, Mekelle Ethiopia (39.2%) [11], probably this difference was due to MAGH health professionals were more adhered to the updated STG of Ethiopia and guide line of ceftriaxone use evaluation.

Most of the inappropriate use was due to inappropriate duration for pneumonia (86.9%) and dose errors for meningitis (13.1%). This is similar with the retrospective cross sectional studies done in Ayder referral hospital, Mekelle, Ethiopia and Dessie Referral Hospital, North East Ethiopia in which most of inappropriate uses of ceftriaxone were seen in terms of duration [11,12]. However the prospective study done in the medical and emergency wards of Gondar university referral hospital, Ethiopia showed that majority of inappropriate ceftriaxone use emanated from inappropriate frequency of administration [15]. This difference is possibly due to the maximum number of patients treated at referral hospital than general hospital which might cause disturbance of drug administration.

The mean duration of ceftriaxone therapy was 8 with the higher range of 2-7 days which was almost similar with the study done in Navodaya Medical College in which most of ceftriaxone treatment was in the range of 3- 6 days [16]. However, it is shorter than that obtained in Gondar University referral Hospital (11.5 days) [15]; this difference was might be the duration of pneumonia treatment is lower in MAGH. But longer than Ayder referral hospital: which was 7.2 days [11] and Dessie referral hospital: which was 6.8 [12]. Probably this is due to poor adherence to STG in MAGH or because hospital acquired pneumonia is high in MAGH.

Corticosteroids were the most frequently co-administered medications. This is not complementary with the retrospective cross sectional studies done in the internal medicine wards of general hospitals in Addis Ababa and Felege Hiwot Referral Hospital (FHRH), Bahir Dar, North Ethiopia, in which maintenance fluids were the most commonly co prescribed medications [17,18]. This might be due to the reason that intensive care units, where maintenance fluids used mostly, are more available in general hospitals of capital city of the country, Addis Ababa, and in referral hospital, FHRH.

The most daily dose, frequency of administration and duration of treatment with ceftriaxone were 1 gm (73.4%), twice daily (73.4%) and 2 to 7 days (83.9%) respectively. This is similar with the study done in the case of Ayder referral hospital, Mekelle, Ethiopia [11]. However, the prospective study done in TASH showed that the most common daily dosage, frequency of administration and duration of treatment with ceftriaxone were 2 g (88.9 %), twice-daily (98.4 %) and 8-14 days (46.2 %), respectively [13]. This difference may be ought to number of critical cases referred to TASH, which may require high dose relatively for a prolonged duration of treatment.

Greater than half of patients were hospitalized in medical ward for a period of 4-7 days which is almost similar with the study done in medical ward of Dessie referral Hospital, Dessie-Ethiopia [12]. More than three-fourth, 79.4%, of subjects were improved at the end of treatment.

Conclusion and Recommendation

Conclusion

Ceftriaxone was mainly prescribed for pneumonia, followed by Meningitis, and UTI, in the majority of the patients' ceftriaxone was inappropriate in duration, followed by dose and frequency, mostly ceftriaxone was given one gram BID among two hundred ninety six, whereas it was two gram BID in among one hundred seven.

For about three hundred eighty eight cases ceftriaxone regimens were given for the period of two to seven days, followed by eight to fourteen days. Most of the patients were improved and discharged from the hospital, four to seven days were the most frequently hospital stay.

Recommendation

In order to improve the rational use and to prevent the development of resistance of ceftriaxone; the health center should prepare and implement updated guide line on the use of ceftriaxone. The DTC should regularly monitor ceftriaxone use evaluation. The health professional should adhere to the updated guide line on the use of ceftriaxone.

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