



Paper Title Drug Use Evaluation of Ceftriaxone in Nifas Silk lafto Worda-01 Health center In Patient Ward, Addis Ababa, Ethiopia

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Background

Ceftriaxone is one of the most commonly used antibiotics due to its availability, wide spectrum of activity and low toxicity. However, irrational use of ceftriaxone is one of the current issues in most countries, especially developing ones.

Objective

The aim of this study was to evaluate ceftriaxone utilization in INPATINT wards of Nifas silk lafto worda-01 HC in Ethiopia.

Methods

An institution-based retrospective cross-sectional study was conducted on randomly selected, patients who were admitted to NSLW01HC from TIRE 2016 to MAGBATE 2016E.c. A structured data abstraction format was used to collect data from patients' Card patient. Medscape® drug interaction checker was used to identify significant drug–drug interactions, and national and international guidelines, STG, EPHCCG, were used to evaluate the appropriateness of ceftriaxone use..

Results

Among the 103 patients enrolled, ceftriaxone was utilized by 53 (51.7%) patients, and these patients were considered for evaluation of appropriateness and subsequent analysis. Among 53patients, ceftriaxone was used for empiric therapy in 47 (60.2%) patients; of which, were for prophylaxis 10 (99.2%) ,In the majority of the patients, the dose of ceftriaxone was 1g/day 472 (78.6%) and for a duration of 2–7 days 409 (68.1%). Inappropriate use of ceftriaxone was observed among 237 (39.4%) patients with regard to indication, dose/frequency and duration. About half (49.3%) of the deviation from the guidelines was observed from surgical and gynecologic/obstetrics wards. Among the co-prescribed medications with ceftriaxone, ringer lactate, Vitamin B Complex and were found to have a significant drug–drug interaction.

Conclusion

This study revealed that inappropriate use of ceftriaxone was high in NSLW01HC. This may increase the emergence of resistant pathogens which may lead to treatment failure and increase cost of therapy. Therefore, adherence to current evidence-based guidelines is recommended.

Keywords: antimicrobials, ceftriaxone, drug use evaluation; DUE, Ethiopia

1. Introduction

Antimicrobials have played a remarkable role in public health through decreasing of morbidity and mortality.¹ The 19th and 20th centuries were peculiar in that health and longevity of populations progressed as the result of substantial achievements in controlling infectious diseases. This however, was not without challenges.²

The wide spread of misuse together with the emergence of antimicrobial resistance and escalating unwanted expenditures have resulted in antimicrobials being the drug most frequently chosen for drug use evaluation (DUE) studies.³ Ceftriaxone, as the most frequently used drug among the third generations cephalosporin class with reputable broad spectrum activity and utilization in many developing countries,⁴ was also highly prone to such problems. Studies reported that ceftriaxone was most often prescribed before culture and sensitivity tests and accurate decision was made in the diagnosis process.⁵

A high rate of inappropriate use of ceftriaxone (87.9%) and impacts of antimicrobial resistance was documented in the world including the developing countries like Ethiopia.⁵ A high rate of ceftriaxone resistance among gram negative bacteria was also reported across the European Union member states, which resulted in extra numbers of cases of infection, deaths, and hospital days.³

Inappropriate indication, empiric or prophylactic therapy and multiple drug uses were associated with misuse of antibiotics⁶ and findings in German indicated a dramatic 10 fold increase in *E. coli* resistance to 3rd generation cephalosporin including ceftriaxone.⁷ Ceftriaxone resistance was also reported among *E. coli* (86.1%) and *K. pneumoniae* (95.8%) in Sudanese general hospital.⁸

In Ethiopia, though there were no comprehensive nationwide studies to demonstrate the magnitude and direction of the problem, a few fragmented studies have documented the threatening incidences of inappropriate use of ceftriaxone. It was reported that there was an increasing rate of ceftriaxone utilization with a high rate of inappropriate use with regard to indication, presence of drug interaction, absence of lab investigation, duration of treatment and dosage regimen.^{5,9,10} This in turn was also associated with fueling an ever-increasing need for a newer antibiotics. Therefore, prudent prescribing of antimicrobial drugs is essential as it may reduce incidences of antimicrobial drug resistance.¹¹

The literature review showed that the previous findings of ceftriaxone utilization in Ethiopia were a small sample size, in limited clinical settings, and evaluated the appropriateness against the Ethiopian standard treatment guideline developed for general hospitals. So, the use of a more rigorous evaluation tool, displaying the magnitude of the problem in a large sample size involving all clinical departments in a facility level is more reliable. Therefore, the objective of this study was to evaluate ceftriaxone utilization in INPATIENT wards of Nifas silk lafto w-01 HC (NSLW-01HC), Addis Ababa, Ethiopia.

2, Materials and Methods

2.1 Study Setting

The study was conducted in newly organized institution at Nifas Silk Lafto around lebu area, woreda- 01 health center, A.A city administration, capital city of Ethiopia, its giving services for all surrounding population and other patients coming from the surrounding woreda and, in and out patient wards, IMNCI, ART, VCT, Delivery w laboratory, pharmacy, emergency service, injection room and health extension programs with having a total of 215 employers, from those 129 health professionals, of this 9 pharmacists, 10 midwives, 9 lab., 48 nurses, 18 HO, 5 Gp and 57 Health Ext, other administrative employers including HRM employers, secretaries, finances, cleaners.... Generally, A.A city has many known referral hospital including private hospitals, governmental health center, private health center with this and others it helps its population accordingly. Obviously A.A city is beautiful city as capital city of Ethiopia than others throughout Ethiopia.

2.2 Study Design

An institution-based retrospective cross sectional study design was employed to evaluate ceftriaxone utilization by reviewing medical records of patients who received ceftriaxone during TIRE 2016 to MAGBATE 2016. The DUE was made against the criteria of the currently developed protocol regarding the rational use of ceftriaxone. The treatment protocol was prepared by compiling current evidence-based recommendations regarding the use of ceftriaxone from WHO guidelines, Ethiopian standard treatment

guideline for general hospital (STG 2014)¹² and Infectious Disease Society of America (IDSA). STG 2014, which is a comprehensive guideline, used in Ethiopian general hospitals for the management of majority of diseases including surgical prophylaxis was extensively used for the protocol preparation. Medscape (Medscape). Traven Health Analytics Inc) drug interaction checker was used to identify drug interactions. It is online application that provides evidence-based medical information including drug–drug interaction.

Source and Study Population

All patients admitted to NSLW-01HC constituted the source population. The study population was all patients admitted to NSLW-01HC during the study period and prescribed with at least 1 dose of ceftriaxone

Sample Size Determination and Sampling Procedure

Small samples of 109 patients' medical charts were reviewed to get the assumed minimum samples that used ceftriaxone. However, among 109 medical charts reviewed 53 (51.7%) were found to use ceftriaxone and considered for evaluation ceftriaxone use appropriateness and subsequent analysis.

2.3 Data Collection and Analysis

Data was collected by 1 trained pharmacist through patients' inpatient ward chart review by using patient data abstraction tool. The content of the data collection tool was designed to record patient information, disease condition, working diagnosis, abnormal laboratory tests, abnormal diagnostic results, culture and sensitivity results, information regarding administration of ceftriaxone including its indication, dose, frequency of administration, duration of therapy, and information regarding co-administered medications. Five criteria, namely indication for use, dose, frequency of administration, duration of treatment, and drug interaction were used to evaluate appropriateness of ceftriaxone utilization based on the prepared protocol. After checking the completeness and appropriateness, the data was entered and analyzed by using Statistical.

3. Results

3.1 Socio-Demographic Characteristics and Clinical Information of Patients

Among the 103 patients enrolled, ceftriaxone was utilized in 53(51.7%) patients and these patients were considered for evaluation of appropriateness and subsequent analysis. The mean \pm SD age of the study participants was 35.0 ± 17.7 years ranging from 3 months to 89 years. The majority (50.9%) of the patients were female and more than two thirds (71.1%) did not have any chronic co-morbidities. Among the study participants, 40 (75.7%) had at least one type of routine investigation which was done before or during ceftriaxone therapy. CBC test 40 (75.4%) was the most frequently conducted investigation followed by CBC 12 (22%).

. Among 53 patients, ceftriaxone was used for therapeutic purpose in 40 (75.4%) patients with empiric therapy and the rest 13 (24.5%) was used for prophylaxis. The prophylaxis uses were commonly for surgical prophylaxis but it was also used among a few patients who had soft tissue injuries.

The mean duration of ceftriaxone treatment was 5.2 ± 3.8 days (ranging from 1 to 90 days). Majority (52.8%) of the patients were treated for 2–7 days and, 25 (62.5%) took ceftriaxone for more than 1 days. For the majority (29; 54.6%) of the patients, the dose of ceftriaxone was 2g/day (50 mg/kg/day for pediatric age groups), followed by 1g-2g/day among 12 (22.6%) patients and less than 1g 12(22.6) (Table 1).

Table 1

Socio-Demographic Characteristics and Clinical Information of Patients in nsLW01HC, June, 2016
(n=53)

Variables		N (%)
Gender	Male	23 (49.7)
	Female	27 (50.3)
Age	3 months to 14 years	23 (43.7)
	14–65 years	27 (50.5)
	Above 65 years	6 (11.8)
Having chronic co-morbidities	Yes	5 (11.1)

Variables	N (%)
No	48 (90.5)
CBC tests	40 (75.5%)
Urine analysis tests	2 (3.7%)
No lab	11 (20.1%)
Duration of ceftriaxone therapy	
Single dose	25 (47.1)
One day (2 doses)	29 (54.5)
2–7 days	12 (22.5)
Daily dose of ceftriaxone utilized	
2g/day	29 (22.5)
1g–2g	12 (22.6)
<1gm	12 (22.8)
Reason for prescribing ceftriaxone	
Therapeutic use	40 (75.2)
Prophylactic use	13 (24.8)

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Maintenance fluid, diclofenac, and metronidazole were the top 3co-medications prescribed among 290 (48.2%), 220 (36.6%) and 74 (12.3%) patients respectively ([Table 2](#)).

Table 2

Top 10 Drugs Frequently Co-Prescribed with Ceftriaxone in NSLWO1HC, 2016 (n=53)

Drugs	Frequency	Percent
Maintenance fluids	40	75.4
Diclofenac	5	9.4
Tramadol	3	5
Cimetidine	2	3
Paracetamol	10	18
AZIROMCYCIN	26	49
SALUBUTAMOLE	12	22.4
Furosemide	2	3.7
Metoclopramide	14	2.6

Indication of Ceftriaxone Use and Compliance to National and International Guidelines

Regarding compliance to guidelines on ceftriaxone utilization, 36(67.6%) of the samples were found to agree with the recommendations set in the guidelines. The rest (13; 24.6%) of the ceftriaxone use was not consistent with the guidelines. Among the top 10 indications for which ceftriaxone was prescribed, for ceftriaxone use were pneumonia (29; 68.9%), acute febrile illness (AFI) (2; 50%) and urinary tract infection (UTI) (9; 9%) ([Table 3](#)). Ceftriaxone was prescribed for AFI, AGE, wound, bronchial asthma, stroke and peptic ulcer disease which were not recommended by the guidelines as eligible indication.

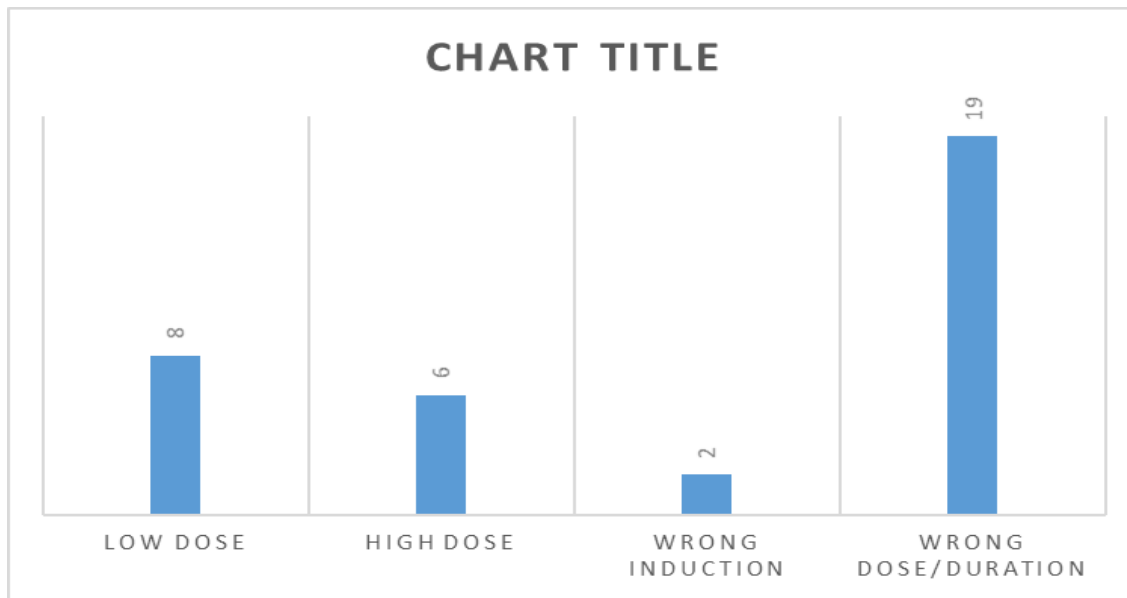
Table 3

Common Conditions for Which Ceftriaxone Was Prescribed and Respective Compliance to the Guidelines in NSLWO1HC, 2016 (n=53)

Assessments	Overall Use		Compliant to the Guidelines	
	N	n	%	
Pneumonia	29	20	68.9	
AFI	2	1	50	
UTI	9	9	100	
AGE	2	1	50	
STIs	3	1	33.3	
Tonsillitis	4	3	75	
Bronchial asthma	7	5	71.5	
Total	53	40	75.4	

Abbreviations: AGE, acute gastroenteritis; AFI, acute febrile illness; UTI, urinary tract infection; STI, sexually transmitted infection; UGIB, upper gastrointestinal bleeding.

. Similarly, incorrect indications and unacceptable duration of therapy for certain diagnosis composed the subsequent higher rate of the noncompliant cases (88; 36.9% and 20; 7.6%). Regarding the general categories of inappropriate ceftriaxone use, unaccepted use for prophylaxis (120; 50%) and wrongly indicated (2; 36.7%) were the major problems identified in this study ([Figure 2](#)).



[Figure 2](#)

Categories inappropriate ceftriaxone utilization in NSLW01HC, 2016 (n=53).

Potential Drug–Drug Interaction among Drugs Co-Prescribed with Ceftriaxone

Among total of 46 drugs checked for potential drug–drug interactions with ceftriaxone, 4 drugs were shown to have amoderate interaction that needs monitoring. The drug interactions were identified among 54 (9%) of the participants with ringer lactate 21 (3.5%), doxycycline 16 (2.7%), heparin 13 (2.2%).

4. Discussion

This study was designed to evaluate the appropriateness of ceftriaxone utilization in NSLW01HC. The current study revealed that a high rate (55.7%) of ceftriaxone utilization was observed. Similar findings of high rate of ceftriaxone utilization (58%) was reported in a study conducted in Tikur Anbessa specialized hospital, Ethiopia.⁵ High rate ceftriaxone utilization was also reported by other studies and the reasons might be attributed to its availability, effectiveness, broad spectrum and low toxicity rates.⁸ In Ethiopia ceftriaxone is the cheapest and commonly available parenteral antibiotics.

The mean duration of treatment in this study was 1.8 days (ranging from stat to 90 days) in fact more than 28(68.1%) of the patients were treated for 2–7 days. The duration was lower than the findings reported from Ayder referral hospital 7.2 days⁸ and Tikur Anbessa specialized hospital.⁵ The shorter duration of therapy in this study might be due to this study included patients in surgery ward that needs short duration of therapy for prophylaxis and a more frequent step down switch of ceftriaxone (intravenous) to other (oral) antimicrobials. The median duration treatment in Victorian was also found to be only 1 days¹⁹ which is shorter than the median of the present study. The discrepancy could be attributed to difference in treated disease conditions and hospitals' protocols used to switch intravenous antibiotic to oral. Generally shorter

duration of intravenous therapy would be desirable in most cases to reduce hospital stay and cost.²⁰ However, severity and site of infection, numbers of comorbidities and patients' response to alternative oral regimens are important before making the decision.

In this study, the most common indications of ceftriaxone use were and pneumonia (68.8%). Similarly, preoperative prophylaxis and pneumonia were the common indication of ceftriaxone use in the findings of Ayder referral hospital¹⁰ and Dessie referral hospital.²¹

In this study, the most frequent daily dose of ceftriaxone was 2g (52.6%) which is in line with the finding of Ayder referral hospital.¹⁰ However, a higher rate of dose of 2g/day was reported from a study in Tikur Anbessa hospital (88.9%).⁵ The discrepancy could be due to the latter study did not include pediatric patients in which a lower daily dose of ceftriaxone was used. This dose was commonly used in Ethiopia for most cases and empiric therapy except for diseases that requires a higher dose, such as meningitis and infective endocarditis.

The inappropriate use of ceftriaxone in this study was found to be 39.6%. This finding was with inline Dessie Referral Hospital 46.2%,²¹ but lower than the findings of Tikur Anbessa specialized hospital (87.9%),⁵ in Iran (85.3%),²⁰ and Ayder Referral Hospital (64.2%).¹⁰ The discrepancy of the findings might be attributed to a retrospective nature of the present study and the differences in the guidelines used to conduct the DUE. The other reason could be that, unlike this study, the above studies were conducted in referral hospitals in which treatment is complicated with several possible inappropriate medication uses. In addition, drug interaction in this study was not considered as inappropriate utilization that will lower the rate of inappropriate ceftriaxone utilization.

In addition, ceftriaxone was utilized for conditions without clear indications like patients diagnosed with AFI, wound, AGE, and bronchial asthma which were not supported in the guidelines.

Maintenance fluid, diclofenac, and metronidazole were the 3 commonly co-administered medication with ceftriaxone. Among drugs concomitantly administered with ceftriaxone, ringer lactate (21; 3.5%) (16; 2.7%), had a potential drug–drug interaction. Co-administration with heparin and warfarin may increase the risk of bleeding. Similar studies were reported in a study conducted in Tikur Anbessa specialized hospital.⁵

4.1 Limitation of the Study

Despite the large sample size in most departments, it was a retrospective cross-sectional study that may under estimate the rate of inappropriate use of ceftriaxone. In addition, the evaluation was relied merely on the patients' medical records for which practices might have actually been different.

4.2 Conclusion

The majority (18.8%) of patients admitted to NSLW01HC utilized ceftriaxone commonly for empiric therapy and prophylaxis purpose. Inappropriate use of ceftriaxone with regard to indication, dose/frequency and duration remains significant. This may increase the emergence of resistant pathogens which leads to treatment failure and increased cost of therapy. Therefore, adherence to current evidence-based guidelines is recommended. Few medications were also found to have a significant drug–drug interaction that requires a close monitoring or avoiding the concomitant administration.

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