

Original Article



The Use of Ceftriaxone in Academic Emergency Departments: Evidence-Based Utilization or Overuse

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Abstract

Background: Nowadays, ceftriaxone is being used widely and its use is less compatible with the current guidelines. The aim of this study was to determine the appropriate use of ceftriaxone. The results may help to find a way to prevent its inappropriate use in the emergency department (ED).

Methods: In this observational-analytical study, the patients who were referred to EDs of two teaching hospitals from September 23, 2019, to March 19, 2020, and treated with ceftriaxone were analyzed. The appropriate use of ceftriaxone was determined based on the latest evidence-based literature.

Results: Ceftriaxone had been prescribed properly in 156 patients (38.4%; 95% CI, 33.5-42.9%) and its use did not meet logical criteria in the remaining 250 patients (69.6%; 95% CI, 57.1-66.5%). The appropriate use of ceftriaxone was independently related to goal-directed use, level I triage, urinalysis (U/A) indicating urinary tract infection (UTI), and chest radiographic evidence of pneumonia.

Conclusion: Our study revealed the inappropriate use of ceftriaxone in teaching medical centers; therefore, further education seems to be necessary in this field.

Keywords: Antibiotic, Guideline, Academic, Antimicrobials, ESI

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Introduction

Antimicrobials have an important role in human health by reducing mortality and morbidity (1). Ceftriaxone is one of the most common antimicrobials prescribed empirically in the emergency department (ED) (2). Its vast domain of activity, long half-life, and low rate of complications have made it a drug of choice in many circumstances in patients suspected of any infection in EDs (3). Nowadays, it is being used frequently, and its use is less compatible with current guidelines most of the time for the general use of antimicrobials (4). It is more frequently used for respiratory, intra-abdominal, and urinary tract infections (UTIs) (2). Many published papers indicate that the most common indication for ceftriaxone use is respiratory infection (4). Inappropriate use of antimicrobials can lead to the resistance of microorganisms to them, which can threaten health system seriously (5,6). The aim of this study was to investigate the logical and non-logical uses of ceftriaxone in EDs, the results of which may help to find a way to prevent its inappropriate use in ED.

Materials and Methods

Study Design and Participants

In this observational-analytical study, the patients who

were admitted to the EDs of two teaching hospitals from September 23, 2019, to March 19, 2020, and treated with ceftriaxone were analyzed. The patients whose data had not been correctly recorded and patients without any indication or contraindication to use ceftriaxone were excluded from the study. A total of 406 patients were enrolled in the study.

Study Protocol

Data were collected from the patients' files during the study period. Patients referred to the two university hospitals (Hazrat Rasool and Firoozgar) during the above-mentioned time entered the study. The appropriate use of ceftriaxone in these patients was evaluated according to the indications mentioned in the valid scientific references (the latest version of UptoDate at the time of study, version 21.6). Data were gathered via history taking, physical exams, and para-clinical evaluations of each patient. The final decision about the appropriate or inappropriate prescription of ceftriaxone was taken by consensus of three specialists (Infectious Disease, Emergency Medicine, and Clinical Pharmacologist) according to patients' data and evidence-based literature. Empiric therapy refers to the prescription of ceftriaxone based on symptoms and



signs of patients and if the treating physicians considered results of para-clinic studies such as chest radiography or urinalysis (U/A), goal-directed therapy was done.

Data Analysis

Data were analyzed using SPSS version 18.0. Quantitative variables were reported as mean and 95% confidence interval (CI) while frequency and percentage were used to report qualitative variables. For data analysis, *t* test, chi-square test, and ANOVA were applied. Logistic regression was used to determine independent variables that predict the appropriate use of ceftriaxone in ED. *P* values less than 0.05 were considered statistically significant.

Results

Eventually, 406 patients were included in the study. The mean age of patients was 53.88 (95% CI, 51.63-55.96), and the maximum and minimum ages of patients were 91 and 2, respectively. In this study, 206 (50.7%; 95% CI, 45.8-54.9%) patients were women, while 200 of them were men. There was a positive history of antimicrobial use during the last three months in 138 patients (34%; 95% CI, 29.3-38.7%) and 182 patients (44.8%; 95% CI, 33.9-49.8%) were febrile at the time of the visit.

The triage level of the patients according to the Emergency Severity Index (ESI) was determined as follows: level I in 10 patients (2.5%; 95% CI, 1.0-3.9%), level II in 76 patients (18.7%; 95% CI, 15.3-22.7%), level III in 178 patients (43.8%; 95% CI, 38.9-48.5%), level IV in 110 patients (27.1%; 95% CI, 23.2-31.3%), and level V in 32 patients (7.9%; 95% CI, 5.2-10.8%). Additionally, the median triage level of the patients was 3 (IQR, 3-4).

The patients' chief complaints were related to gastrointestinal (GI) tract in 152 cases (37.4%; 95% CI, 32.8-42.1%), respiratory tract in 100 cases (24.6%; 95% CI, 20.4-29.1%), weakness and malaise in 100 cases (24.6%; 95% CI, 20.2-28.8%), and urinary tract in 54 cases (13.3%; 95% CI, 10.1-16.7%).

The evaluation and management of patients had been ordered by emergency physicians (EPs) with different years of training: 34 patients (8.4%; 95% CI, 5.7-11.1%) by post-graduate (PGY) 3 emergency medicine resident (EMR), 82 patients (20.2%; 95% CI, 16.3-23.9%) by PGY 2 EMR, and 290 patients (71.4%; 95% CI, 67.0-76.1%) by PGY 1 EMR.

Patients were divided into six disease groups according to their data: 94 patients (23.2%; 95% CI, 19.0-27.6%) with UTI, 84 patients (20.7%; 95% CI, 16.7-24.9%) with intra-abdominal infection, 78 patients (19.2%; 95% CI, 15.3-22.9%) with pneumonia, 66 patients (16.3%; 95% CI, 12.6-20.2%) with sepsis of unknown origin, 62 patients (15.37%; 95% CI, 11.8-18.7%) with GI infection, and 22 patients (5.4%; 95% CI, 3.4-7.6%) with upper respiratory infection (URI).

Ceftriaxone had been prescribed for prophylactic purposes in 28 patients (6.9%; 95% CI, 4.4-9.6%), while it had been prescribed for therapeutic purposes in 378

patients (93.1%; 95% CI, 90.4-95.6%). Additionally, it had been prescribed empirically in 304 patients (74.9%; 95% CI, 70.9-78.8%) and it had been used as a goal-directed therapy in 102 patients (25.1%; 95% CI, 21.2-29.1%).

Leukocytosis was observed in 128 patients (31.5%; 95% CI, 27.1-36.0%). Additionally, 226 patients had no leukocytosis, while complete blood count (CBC) was not performed in 52 patients (12.8%; 95% CI, 9.6-16.0%). In 78 patients (19.2%; 95% CI, 15.3-23.2%), urinalysis indicated UTI. Besides, abnormalities in the urine test was not significant in 240 patients, and in 88 patients (21.7%; 95% CI, 17.7-25.9%), urinalysis was not requested. Lumbar puncture was done in 4 patients (1%), one of whom indicated infection. The analysis was not performed because of the small number of cases. In 34 patients (8.4%; 95% CI, 5.7-11.3%), chest X-rays (CXRs) were in favor of pneumonia while 236 CXRs (58.1%; 95% CI, 53.4-62.8%) revealed nothing in favor of infection. CXRs were not requested in 136 patients (33.5%; 95% CI, 29.1-38.2%).

According to the current guidelines and consensus of our experts, ceftriaxone had been prescribed appropriately in 156 patients (38.4%; 95% CI, 33.5-42.9%) and its use did not seem appropriate in 250 of them (61.6%; 95% CI, 57.1-66.5%).

Although the prescription of ceftriaxone seemed more appropriate in more experienced EPs (Table 1), it did not reach the significance level ($P=0.068$). No statistically significant correlation was seen between the appropriate use of ceftriaxone and therapeutic or prophylactic intention to use it ($P=0.617$). As it is shown in Table 2, ceftriaxone had been used more appropriately in patients complaining of urinary symptoms ($P<0.001$). Its use was less appropriate when prescribed empirically compared to goal-directed prescription (24.34% vs. 80.4%; $P<0.001$). Moreover, ceftriaxone had been used more appropriately in patients with higher triage levels (level V to level I) ($P<0.001$). Leukocytosis was significantly correlated with the appropriate use of ceftriaxone ($P<0.001$). It was also correlated with the evidence of infection according to urinalysis and CXR (Table 3).

Regression analysis was performed to determine the independent effect of factors on the appropriate use of ceftriaxone in ED. It was found that not-empiric prescription (goal-directed use), triage levels I and II, and urinary symptoms as the chief complaint can predict the appropriate use of ceftriaxone in ED (Table 4).

Discussion

Considering the inappropriate use of ceftriaxone in ED, it seems necessary to follow a guideline to use it logically; however, guidelines would be useful when considering the patient's medical history, physical exam, and ancillary tests (3). Inappropriate and frequent use of ceftriaxone may lead to drug resistance. As it is a wide-spectrum antimicrobial agent, its prescription should be substituted with other narrow-spectrum antibiotics whenever possible to decrease its use and prevent resistance (4).

Table 1. Appropriate Use of Ceftriaxone by Physicians

	PGY 1 EMR	PGY 2 EMR	PGY 3 EMR
Appropriate use of ceftriaxone	35.2%	43.9%	52.9%

PGY: post-graduate year, EMR: emergency medicine resident

Table 2. Appropriate Use of Ceftriaxone According to the Patients' Complaints

Patients' Complaints	Urinary Symptoms	Weakness and Malaise	Respiratory Symptoms	GI Symptoms
Appropriate use of ceftriaxone	66.67%	42%	38%	26.31%

GI: gastrointestinal.

Table 3. Appropriate Use of Ceftriaxone according to Leukocytosis, U/A in Favor of UTI, and CXR in Favor of Pneumonia

	Leukocytosis	U/A in Favor of UTI	CXR in Favor of Pneumonia
Appropriate use	59.37%	97.4%	94.17%
Inappropriate use	33.62%	25.0%	37.28%
Not done	7.6%	22.72%	26.47%

U/A: urinalysis, UTI: urinary tract infection, CXR: chest X-ray

Table 4. Multivariate Analysis Indicating Three Independent Factors Associated with Higher Odds of Logical Ceftriaxone Prescription

	Odds Ratio	95% CI	P Value
Triage levels I and II	10.32	2.3-45.1	0.02
Goal-directed use	13.94	6.1-31.4	0.01
Urinary symptoms as the chief complaint	8.45	1.6-43.1	0.01

CI: confidence interval, CXR: chest X-ray, U/A: urinalysis, UTI: urinary tract infection

In the current study, the rate of the appropriate use of ceftriaxone was recorded to be 38.4%, indicating that it should be used more cautiously.

Waldrop et al assessed the overuse of antimicrobials (e.g., ceftriaxone) by EPs to manage wounds in an urban medical center. During a one-month period, they gathered data from 72 patients and concluded that 31% of cases had received ceftriaxone with no logical indication. It had been affected neither by demographic characteristics of the patients nor by EPs' board certification (7).

Jain et al studied the logical use of ceftriaxone in a pediatric ED in Atlanta and assessed 229 patients who had been referred with fever and had received at least one dose of ceftriaxone in ED. Overall, ceftriaxone had been prescribed 289 times to 229 patients and 60 patients (26% of them) had received two or more doses of ceftriaxone during the study period. The physicians had discovered the primary sources of infection in 180 patients (pneumonia in 76 cases), while sources of infection were unknown in 49 of them. According to the guidelines, ceftriaxone had been prescribed logically in only 48 patients (16.6% of them) and this rate was 13% in 60 patients who had received at least two doses. Authors concluded that ceftriaxone had been used incorrectly in most cases of pediatric emergencies (3).

In another study done in non-emergency departments of a hospital in Ethiopia on 316 patients, ceftriaxone had

been used logically in 170 of them (55.8%) (8). Shimels et al conducted a retrospective study in two governmental and private hospitals in Ethiopia, assessing 447 files. The rate of the appropriate use of ceftriaxone was reported to be 48.9% and 44.6% in governmental and private centers, respectively (9). Phuphuakrat et al observed a 58.3% rate of the appropriate use of ceftriaxone in ED. Factors positively affecting this rate were female gender (odds ratio [OR]=1.96), presence of fever (OR=3.12), and suspected diagnosis of sepsis (OR=7.9), while the diagnosis of GI infection was an independent factor affecting inappropriate use of ceftriaxone (OR=0.2) (2).

Berhe et al assessed the use of ceftriaxone in the medical ward and teaching hospital in 120 patients. They found that 58.9% of patients were treated in the range of 0-7 days. The most common cases of ceftriaxone use were reported to be pneumonia, sepsis, TB, and CHF. Based on the results of this study, ceftriaxone use was appropriate in 30 (27.5%) cases and it was reported to be inappropriate in 68 (62.4%) cases (10).

Sonda et al studied the use of ceftriaxone in a tertiary care hospital on 630 patients, 322 of whom were treated with ceftriaxone during hospitalization. According to the results, predicting factors were identified as history of any medication use before referral to the hospital (OR=3.4, 95% CI: 1.0-11.4, $P=0.047$), bacterial infection (OR=18.0, 95% CI: 1.4-225.7, $P=0.025$), surgical ward (OR=2.9, 95% CI: 0.9-9.4, $P=0.078$) and medical wards (OR=5.0, 95% CI: 0.9-28.3, $P=0.070$). Due to the high consumption of ceftriaxone in Kilimanjaro Christian medical centre (KCMC), it is necessary to monitor and regulate the antimicrobial consumption in the hospital to prevent the rising crisis of antibiotic resistance (11).

In another study, 400 patients were assessed. It was found that 65.5% of the patients had received ceftriaxone appropriately. Pre-operative prophylactic prescription and empiric therapy for fever were the main reasons for the inappropriate use of ceftriaxone (12).

Broad spectrum and long duration of antimicrobial activity have made ceftriaxone a favorable agent in empiric management in many conditions which are not necessarily approved in some situations. In fact, the empiric prescription is one of the most important factors which causes inappropriate use of it (3).

Conclusion

Scientists worry about the frequent and inappropriate use of antimicrobials, especially ceftriaxone (13). Ceftriaxone is a broad-spectrum antimicrobial agent with a low rate of complications and long half-life. Considering the increasing rate of its prescription in many circumstances with no indication, it seems necessary to assess the correct and appropriate use of it in ED and educate physicians about how to use it appropriately and according to validated guidelines to prevent drug resistance.

In the present study, the probability of inappropriate use of ceftriaxone was shown to be higher in patients

with lower acuity of illness (triage level II-V), empiric management, and prescription before performing laboratory and radiologic studies. Moreover, the presence of urinary symptoms as the chief complaint could convince the emergency physician to prescribe ceftriaxone in the first order.

We showed that the rate of logical use of ceftriaxone in ED was not acceptable for an academic center indicating the need for more effective education.

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Competing Interests

The authors declare that they have no conflict of interests.

Ethical Approval

The study was approved by the Ethics Committee of Iran University of Medical Sciences (thesis code:9211307017).

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