Appropriate Use of Ceftriaxone in the Emergency Department of a Veteran's Health Care System

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Abstract

Background: Ceftriaxone is a third-generation cephalosporin commonly utilized as an empiric antibiotic treatment option in the emergency department (ED). Overuse can lead to decreased susceptibility and emergence of multidrug-resistant pathogens, increased costs, and unnecessary adverse effects. **Objective:** The purpose of this project was to determine the appropriateness of ceftriaxone usage in the ED of a veteran's health care system. **Methods:** This retrospective chart review included all veterans who received at least one dose of ceftriaxone in the ED between June 1, 2014, and June 1, 2015. The primary outcome was the percentage of appropriate ceftriaxone use. Usage appropriateness was determined on a case-by-case basis by examining current published guidelines and local recommendations based on the institutional antibiogram. **Results:** Ceftriaxone was prescribed for a wide variety of indications and was determined to be inappropriately prescribed in 164 patients (53%). The most common reason for inappropriate prescribing was lack of a first-line indication for ceftriaxone (64%). Only 120 patients (38.5%) exhibited systemic signs of infection based on vital signs and laboratory parameters, and 25 patients (8%) likely did not require antibiotic therapy at all. **Conclusions:** Ceftriaxone was used inappropriately in more than half of the patients who received the drug in the ED. The literature on the prescribing habits for ceftriaxone is limited in the United States, but these results are similar to studies conducted in other countries. Attempts should be made to educate prescribers on appropriate indications for the use of ceftriaxone.

Keywords

cephalosporins, emergency medicine, drug utilization evaluation, antibiotic resistance, infectious diseases

Introduction

Ceftriaxone is a commonly used third-generation cephalosporin antibiotic. Its pharmacokinetic profile, spectrum of coverage, and tolerability make it an attractive option for use in the emergency department (ED), outpatient clinic, and hospital setting. Ceftriaxone is highly protein bound and thus has a long half-life, which allows it to be administered once daily via the intravenous (IV) or intramuscular (IM) route. It is eliminated through the biliary tract and does not need to be dose adjusted for renal or hepatic dysfunction. Ceftriaxone is active against many commonly encountered gram-positive and gram-negative pathogens, such as *Streptococcus pneumoniae* and *Escherichia coli*, respectively. It has US Food and Drug Administration–approved labeling for bacterial infections such as lower respiratory tract infections, sepsis, meningitis, skin and skin structure infections, bone and joint infections, intraabdominal and urinary tract infections, and pelvic inflammatory diseases.¹ Ceftriaxone remains highly active against many susceptible pathogens and is recommended as a first-line treatment option in many of the infectious diseases guidelines.^{2–7}

Antibiotics are prescribed frequently in the ED⁸; however, they may be overutilized or prescribed for inappropriate indications. Inappropriate use of antibiotics can lead to decreased susceptibility and the emergence of multidrug-resistant pathogens, treatment failure, unwanted adverse effects, and increased costs to the health care system.^{9–11} Literature, specifically on the appropriate empiric use of ceftriaxone, is limited, but several drug use evaluations (DUEs) have shown a range for appropriate ceftriaxone usage of 12.1% to 78%.^{12–17}

At this project site, ceftriaxone susceptibility for multiple organisms was found to have decreased between 2010 and 2014. For example, in 2010, ceftriaxone susceptibility

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to *Escherichia coli* was 97%. By 2014, susceptibility had decreased to 91%. Although susceptibility currently remains high, this decreasing trend is likely to continue with widespread use of ceftriaxone. Due to the aforementioned concerns regarding increasing antimicrobial resistance, assessing the appropriate use of ceftriaxone in the ED was essential as it is a typical location for empiric therapy. The purpose of this project was to determine the appropriateness of ceftriaxone usage in the ED.

Materials and Methods

This quality improvement (QI) project was conducted in the ED of a veteran's health care system that services central Alabama and west Georgia. This was a retrospective analysis that included all patients admitted to the ED between June 1, 2014, and June 1, 2015, who received at least one dose of ceftriaxone. The project was approved by the institutional review board of Auburn University. An electronic report was generated to identify all ED patients for whom a medication order for ceftriaxone was placed during the project period. All data were collected on a standardized data collection form by a pharmacist or pharmacy intern and stored in the pharmacy department. Data collected included age, gender, ethnicity, indication for ceftriaxone, white blood cell count, temperature, chest X-ray, blood and urine culture results, urinalyses, and discharge antibiotics. Descriptive statistics were used to characterize the patient population. The primary outcome measured was the percentage of appropriate ceftriaxone use. Due to the retrospective nature of this analysis, the appropriateness of ceftriaxone was determined on a case-by-case basis by examining current published guidelines and local recommendations based on the 2014 institutional antibiogram. For example, the Infectious Diseases Society of America (IDSA) treatment guidelines for community-acquired pneumonia recommend ceftriaxone as a first-line empiric treatment option for outpatient therapy if the patient has underlying comorbidities, such as diabetes mellitus; it is also recommended for inpatient treatment if the patient does not require admission to an intensive care unit.⁶ If a patient presented to the ED with clinical signs and symptoms of community-acquired pneumonia, had a chest X-ray positive for infiltrates, and a history of diabetes mellitus, it was deemed that ceftriaxone was an appropriate option. However, if a patient presented with symptoms of an upper respiratory infection, no fever, and a negative chest X-ray, the use of ceftriaxone was deemed inappropriate. For the treatment of skin and soft tissue infections, the IDSA guidelines do not recommend ceftriaxone as a treatment option for cellulitis or purulent abscesses.⁷ Thus, if a patient was admitted to the ED and received ceftriaxone for one of these indications, ceftriaxone was deemed to have been inappropriately prescribed. Similar methods of determining appropriateness were used with the other disease

Table 1. Baseline Patient Characteristics.

Baseline Characteristics	Number of Patients (%)
Gender (n = 312)	
Male	269 (86.2)
Female	43 (13.8)
Race (n = 312)	
White	132 (42.3)
Black	170 (54.5)
American Indian	2 (0.06)
Unknown	8 (2.56)
Age (n = 312; mean 58 ± 15.38)	
<60 years	157 (50.3)
≥60 years	155 (49.7)
White blood cell (n = 215; mean 9.74 ± 4.01)	
>10 000 cells/mm ³	86 (40)
Temperature (n = 312; mean 98.48 ± 1.46)	
>100.4°F	33 (10.6)
<95°F	1 (0.003)
Chest X-ray (n = 141)	
Positive for infiltrates	41 (29)
Negative for infiltrates	100 (71)
Blood cultures (n = 64)	
Positive	6 (9.4)
Negative	58 (90.6)
Urine cultures (n = 33)	
Positive	10 (30.3)
Negative	23 (69.7)
Urinalysis (n = 124)	
Abnormal	44 (35.5)
Normal	80 (64.5)

states for which ceftriaxone was empirically prescribed. In addition, concomitant and discharge medications were also evaluated for determining ceftriaxone appropriateness.

Results

A total of 312 patients were included in the analysis. Baseline patient characteristics are shown in Table 1. The majority of the patients assessed were male (86%), African American (54%), and over the age of 50 year (72%; mean 58 ± 15.38, range = 22-96). Ceftriaxone was prescribed for a wide variety of indications, as shown in Figure 1. Only 120 patients (38.5%) exhibited systemic signs of infection based on laboratory parameters, including temperature greater than 100.4°F or a white blood count of >10 000 cells/μL; one patient experienced hypothermia, but no patients experienced leukopenia. More than half of the patients received ceftriaxone inappropriately (164 patients, 53%), as shown in Figure 1. The most common reason for inappropriate prescribing was a lack of first-line therapy indication for ceftriaxone (64%).

Figure 1. Ceftriaxone appropriateness by indication. Abbreviations: URTI, upper respiratory tract infection; LRTI, lower respiratory tract infection; UTI, urinary tract infection; STI, sexually transmitted infection; SSTI, skin and soft tissue infection; GI, gastrointestinal infection; COPDE, chronic obstructive pulmonary disease exacerbation.

Upper respiratory tract infections were the most common indication for prescribing ceftriaxone, with approximately one third of these being considered inappropriate. Almost all cases (89%) of ceftriaxone use for the treatment of skin and soft tissue infections were considered inappropriate, and all ceftriaxone use for chronic obstructive pulmonary disease exacerbations was inappropriate. Twenty-five patients (8%) likely did not require antibiotic treatment as patients exhibited no signs or symptoms and did not have other laboratory or diagnostic markers indicative of a bacterial infection.

The majority of patients were discharged home from the ED (229 patients, 73%), while the remaining were either admitted to the hospital (59 patients, 19%) or transferred to another facility (20 patients, 6.5%). Twenty patients (7%) were discharged from the ED with no prescription for oral antibiotics, indicating that the ceftriaxone administered in the ED was almost certainly not indicated. Only 3 patients were discharged on an oral third-generation cephalosporin. Forty-seven patients (15%) were discharged home with amoxicillin/clavulanate, an antibiotic with a similar spectrum of activity to ceftriaxone. Some patients were discharged with antibiotics that do not have comparable antimicrobial coverage to ceftriaxone, such as trimethoprim/sulfamethoxazole and the tetracyclines. In these cases, based on review of the chart documentation, it appeared that the prescribing clinician thought the patient might have an infection due to methicillin-resistant *Staphylococcus aureus*, which would also mean the ceftriaxone dose was not warranted.

Due to the results of this project, an electronic restriction template for ceftriaxone is currently under development at the project site and will be implemented after completion and final approval by the pharmacy and therapeutics committee.

Discussion

To our knowledge, this is the first study published from the United States that has specifically examined the use of ceftriaxone in the ED setting. The results of this study indicate that ceftriaxone is frequently used inappropriately in the ED. The exact reasons for this remain unclear, but we hypothesize a number of reasons. Ceftriaxone is broad-spectrum, long-acting, well-tolerated, and can be administered IV or IM, all properties which make it an appealing option for quick use in the ED. Several of the patients in this study probably did not require antibiotic therapy at all. The majority of patients were discharged from the ED on oral antibiotics, and many patients likely did not warrant the use of an IV or IM drug.

Although it is likely that ceftriaxone overuse occurs at many other health care institutions, published data on this topic are limited. A recent DUE performed in India to examine prescribing habits in the ED demonstrated that ceftriaxone was the most frequently prescribed antimicrobial agent, although appropriateness was not assessed.⁸ Several DUEs published in Ethiopia have assessed ceftriaxone usage, but results were not confined to the ED.¹²⁻¹⁵ In these studies, overall inappropriate use of ceftriaxone ranged from 39% to 87.9%. Only 2 studies stratified results according to location. One found ceftriaxone was used inappropriately in 16 of 24 patients in the ICU and ED (66.7%).¹⁴ The other found that ceftriaxone was used inappropriately more often in the ED than in the medical ward (90.4% vs 87%, respectively).¹⁵ Two additional articles have specifically evaluated ceftriaxone use in EDs. The results of a study published in Thailand showed that ceftriaxone was inappropriately given in 41.7% of cases.¹⁶ A study from Australia stratified results based on indication and found that ceftriaxone was used inappropriately in 57% of respiratory tract infections, 28% of intraabdominal infections, 22% of urinary tract infections, and 50% of other infections.¹⁷ Overall, these results are similar to what was noted with this QI project, where ceftriaxone was found to be inappropriately used in 53% of patients.

It is important to note that the retrospective nature of this project confers limitations inherent to this type of design. In particular, the determination of appropriateness was made by the authors based on the information provided through chart review. Thus, it is possible that some patients who were classified as having received ceftriaxone appropriately may in actuality have received it inappropriately and vice versa due to interpretation of data and rationale or lack of data and rationale. This project was conducted in a veteran's health care system where protocols are commonly used, but this did not seem to influence our results. However, the patient population and disease states may be different than a traditional community or teaching hospital ED setting, and thus may not be applicable outside of the veteran's health care system.

This project also had a relatively small number of patients due to limiting the review to 1 year. In addition, the patients were predominately older males, making applicability to females and pediatric and young adults patients limited.

Conclusions

The many characteristics of ceftriaxone that make it an appealing antibiotic for easy use in the ED and other health care settings may contribute to its use for inappropriate indications. This project sought to examine the appropriateness of ceftriaxone use in the ED to ultimately improve prescribing practices of this important antimicrobial agent. Overall, ceftriaxone was found to have a high rate of inappropriate use in the ED. Although this is the first report published in the United States, these results are comparable to reports published in other countries. Many patients could have received a more narrow-spectrum, oral antibiotic based on their indication. Judicious and appropriate use of antibiotics is important to minimize the development of multidrug-resistant organisms and for improving patient outcomes, such as minimizing adverse effects and medical costs. Institutions should evaluate their own prescribing patterns of ceftriaxone in order to maintain its usefulness in the antibiotic armamentarium.

Author Contributions

SHD: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

MJW: Contributed to design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

LSE: Contributed to conception; contributed to analysis and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

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