

RESEARCH ARTICLE



Experience with ceftaroline for treatment of methicillin-resistant *Staphylococcus aureus* pneumonia in a community hospital

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ABSTRACT

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) is an organism causing significant mortality and morbidity with nosocomial infections. Ceftaroline is a new cephalosporin antibiotic that has activity against MRSA. In the USA, this antibiotic has not been approved for use in pneumonia caused by MRSA.

Objectives: To review the use of ceftaroline in MRSA pneumonia in a US hospital and evaluate its clinical success.

Methods: A retrospective study was conducted in an urban community hospital assessing the use of ceftaroline for MRSA pneumonia.

Results: The clinical success was comparable to the currently approved treatment for MRSA pneumonia.

Conclusion: The results of our study showed a favorable result for the treatment of MRSA pneumonia. Well-designed studies need to be performed for further validation of these results.

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1. Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important cause of nosocomial pneumonia with significant morbidity and mortality. It is an uncommon cause of severe community-acquired pneumonia (CAP), where it may affect previously healthy adults and present with necrosis. Commonly used antimicrobial agents used to treat this infection include vancomycin and linezolid. Increasing minimum inhibitory concentrations of vancomycin in MRSA treatment have led to concerns over its reduced efficacy in the treatment of pneumonia [1–3]. Other, less than ideal alternatives include tigecycline and telavancin [4].

Ceftaroline fosamil is a broad-spectrum cephalosporin with enhanced activity against Gram-positive organisms including *Staphylococcus aureus*. It is approved in the USA for the treatment of acute bacterial skin and skin structure infections (ABSSI), including those caused by MRSA. It is also approved for the treatment of community-acquired bacterial pneumonia, including that caused by methicillin-susceptible *S. aureus*. Approval for its use in pneumonia was based on randomized double-blinded trials in which ceftaroline was compared to ceftriaxone [5]. Treatment of MRSA pneumonia was not evaluated in these studies and ceftaroline is currently not approved for this indication in the USA.

Ceftaroline represents a potentially attractive alternative agent for the treatment of MRSA pneumonia. Physicians are comfortable with cephalosporins,

including their efficacy, safety profile, and minimal drug interactions. Given the efficacy of ceftaroline in the treatment of MRSA in ABSSI, it has been used off label in the treatment of other MRSA infections. Case reports describe its use in MRSA pneumonia, including those where vancomycin has failed [6]. A retrospective, matched, case-control study, published in 2016, on MRSA hospital-acquired pneumonia and healthcare-associated pneumonia (HCAP) that included 40 patients treated with ceftaroline suggested benefits over older agents [7].

We reviewed our hospital's experience with the use of ceftaroline in MRSA pneumonia and evaluated its clinical success. It is hoped that this study will add to the growing body of literature regarding the clinical utility of ceftaroline for this infection and help to inform clinical decisions in the absence of randomized controlled trials.

2. Materials and methods

A retrospective chart review was conducted on adult patients at a community hospital serving a diverse patient population in the New York City between January 2014 and March 2016, using electronic medical records (EMRs). Patients who received ceftaroline for MRSA pneumonia were included in the review. All patients were included regardless of whether they had CAP, HCAP, or ventilator-associated pneumonia (VAP). Inclusion criteria included

radiological evidence of pulmonary infiltrate and sputum and/or blood culture positive for MRSA. Patients were excluded if they received <7 days of ceftaroline. All the samples obtained for sputum culture had fewer than 25 squamous epithelial cells per low-power field and were adequate samples.

Data collected from patients' EMRs included demographic characteristics, comorbid conditions, microbiological data, imaging findings, and laboratory data. Patients were categorized as having CAP, HCAP, and VAP according to previously published guidelines from the American Thoracic Society and Infectious Diseases Society of America [8,9].

All antibiotic therapy including prior and concurrent use was recorded. Outcome measures included clinical success, hospital and intensive care unit (ICU) lengths of stay after diagnosis of MRSA infection, mortality, 30 day readmission rate, and adverse drug reactions.

Clinical success was defined as the resolution of signs and symptoms of infection at the end of ceftaroline therapy as documented by the treating physician. Treatment failure was defined as any of the following: (i) persistent signs and symptoms of infection at the end of ceftaroline therapy; (ii) death that could be attributed to ongoing infection; or (iii) adverse drug reaction requiring cessation of ceftaroline treatment. Indeterminate outcomes were defined as those lost to follow-up and death from causes other than pneumonia.

Descriptive statistics were used in analyzing the data. Descriptive characteristics are reported as percentages and mean or median values.

3. Results

Demographic and clinical characteristics including outcome measures are summarized in Table 1. Twenty-five patients (81%) had a diagnosis of HCAP, six (19%) CAP, and none of the patients had VAP. Sixty-one percent of patients required mechanical ventilation and 65% required admission to an ICU.

Clinical success was achieved in 19 patients (62%) and treatment failure in six patients (19%), and five patients (16%) had indeterminate outcomes. There were six deaths (19%), five of which were related to infection. Of the 11 patients with concomitant bacteremia, six (55%) were clinical successes, four (36%) were failures, and one (9%) was indeterminate.

Seven of the patients (23%) received concurrent anti-MRSA therapy other than ceftaroline. Ceftaroline in these patients was added on when there was no clinical improvement on other MRSA therapy. Of the seven patients, five achieved clinical cure, one patient had failure, and one was indeterminate. No allergic reactions or adverse events were recorded as being clearly linked to ceftaroline use and it was never discontinued because of this concern.

Table 1. Clinical characteristics of patients with methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia included in the study ($N = 31$).

Characteristic	
Age (years)	
Median (range)	72 (35–94)
Mean	69.6
Gender	
Male	22 (71)
Female	9 (29)
Ethnicity	
Hispanic	11 (35)
Non-Hispanic	20 (65)
Comorbidity	
Malignancy	3 (9)
Chronic lung disease	11 (35)
Diabetes mellitus	16 (52)
Renal failure	5 (16)
Liver failure	1 (3)
Heart disease	2 (6)
Immunosuppression/AIDS	2 (6)
Result of sputum culture	
Only MRSA	14 (45)
<i>Candida</i>	4 (13)
<i>Bacillus</i> species	3 (10)
<i>Klebsiella</i>	3 (10)
Other	7 (22)
Outcome	
Clinical success	19 (62)
Death	6 (19)
Hospital length of stay (days), mean	25.6
ICU length of stay (days), mean	12
30 day readmission	03 (9)

Data are shown as n (%) unless otherwise indicated.

AIDS, acquired immune deficiency syndrome; ICU, intensive care unit.

4. Discussion

MRSA pneumonia is difficult to treat with currently available antibiotics. The literature reports success rates of less than 60% with standard therapy such as linezolid and vancomycin [10].

There are case reports and case series documenting the use of ceftaroline in patients with a variety of severe MRSA infections as a rescue therapy after failure of vancomycin or daptomycin [11]. Ceftaroline has also been used for bacteremia as well as endocarditis, with good results [12]. A retrospective case-control study, published in 2016, evaluated its use in MRSA pneumonia [7]. The present study was undertaken to review our institution's experience with ceftaroline in the treatment of MRSA pneumonia.

In our study, clinical success was achieved in 62% of the patients receiving ceftaroline for MRSA pneumonia. Of the patients with concomitant bacteremia, 55% were clinical successes. These results compare favorably to previously published success rates with currently approved therapy for MRSA pneumonia. The studies comparing linezolid and vancomycin for MRSA pneumonia have not shown the superiority of one drug over the other [13]. The renal toxicity of vancomycin [14] and the drug interactions associated with linezolid [15] are well known. Ceftaroline is a promising option for the treatment of MRSA pneumonia and bacteremia. As a cephalosporin, ceftaroline has a relatively good safety profile with low potential for drug interactions. The

major side effects are nausea, headache, diarrhea, and pruritus [16].

Limitations of our study include its retrospective design and the confounding effects of prior and concurrent antibiotics on the outcome. Its single-center design may affect the generalizability of the results.

These data suggest that ceftaroline may be useful as an alternative therapy for MRSA pneumonia. Further research, including larger controlled trials, is warranted.

5. Conclusion

In summary, in this retrospective case series, ceftaroline was relatively effective and well tolerated in patients with MRSA pneumonia. A cephalosporin with an acceptable safety profile and good tissue penetration would be a welcome addition to the armamentarium for the treatment of MRSA pneumonia. Large prospective trials are indicated to better establish the role of ceftaroline in the treatment of severe MRSA infections, including the optimum dosing and duration of therapy.

Disclosure statement

No potential conflict of interest was reported by the authors.

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