Case Report

Ceftriaxone for the Treatment of Methicillin-susceptible *Staphylococcus aureus* Bacteremia: A Case Series

Rachel Amanda Lowe, Katie Elizabeth Barber, Jamie Leigh Wagner, Allison Miriam Bell-Harlan, Kayla Renay Stover

Department of Pharmacy Practice, School of Pharmacy, University of Mississippi, Jackson, MS 39216, USA

Abstract

Methicillin-susceptible *Staphylococcus aureus* (MSSA) causes 45% of *S. aureus* bloodstream infections (BSI) and is the most important cause of BSI-associated death. The standard of care therapy is an anti-staphylococcal penicillin or cefazolin, but dosing frequencies for these agents are often infeasible; multiple daily doses tie up infusion lines and are impractical for outpatient antibiotic infusion. Ceftriaxone represents a promising alternative, with once daily dosing and a short infusion time. Currently, treatment with ceftriaxone for invasive MSSA infections is infrequent, with minimal data supporting the clinical utility of ceftriaxone for MSSA BSI. In this case series, we identified 15 patients receiving ceftriaxone for treatment of MSSA BSI, either following standard of care therapy or as initial therapy. Patients were evaluated for clinical cure (CC)(clearance of BSI and normalization of white blood cell count) and microbiological cure (MC)(clearance of blood cultures and no recurrence of organism within 60 days). CC was observed in seven patients, with MC observed in all patients. Only one patient was readmitted to the hospital. This case series provides vital data to support ceftriaxone for treatment of MSSA BSI. With few readmissions and recurrences of infection, ceftriaxone was an effective option for maintenance therapy after resolution of the BSI. Ceftriaxone appears to be a viable alternative for the treatment of MSSA BSI.

Keywords: Bacteremia, beta-lactam, ceftriaxone, infectious diseases, methicillin-susceptible *Staphylococcus aureus*

Introduction

Staphylococcus aureus is a leading cause of bloodstream infections (BSI) and BSI-associated death.[1] The incidence of methicillin-susceptible *S. aureus* (MSSA) was 24.2/100,000 persons in 2013; the case fatality ratio was 20.2%.[2,3] Standard of care, first-line therapy options for MSSA BSIs are anti-staphylococcal penicillins or cefazolin.[4-7]

Ceftriaxone which has in *vitro* MSSA susceptibility (95%–100% susceptible),[8-10] is relatively inexpensive, has a long half-life enabling once-daily dosing, and does not require dosage adjustments in renal dysfunction, making it a viable alternative option.[6] Despite this, ceftriaxone treatment for invasive MSSA is infrequent. Since minimal data support ceftriaxone for these infections, our objective was to report clinical outcomes for MSSA BSIs treated with either standard of care therapy (SOCT) followed by ceftriaxone or ceftriaxone initially. Clinical cure (CC) was defined as clearance of BSI and normalization of white blood cell count (WBC) and temperature within 7 days of the first positive blood culture. Microbiological cure (MC) was defined as clearance of blood cultures and no repeated organism isolation within 60 days.

Access this article online

Quick Response Code:

Website: www.jpharmacol.com

DOI: 10.4103/jpp.JPP_5_17

Case Reports

Case 1

A 74-year-old male admitted for altered mental status from an outside hospital (OSH) had a past medical history (PMH) of diabetes mellitus (DM), diabetic retinopathy, and atrial fibrillation. Blood and urine cultures revealed MSSA, and treatment was de-escalated from vancomycin to ceftriaxone 2 g every 24 h on day 3. Transesophageal echocardiogram (TEE) revealed no vegetations, but an epidural abscess was identified on day 4. Magnetic resonance imaging (MRI) revealed septic

Address for correspondence: Katie Elizabeth Barber, Department of Pharmacy Practice, School of Pharmacy, University of Mississippi, 2500 North State Street, Jackson, MS 39216, USA.
E-mail: kbarber@umc.edu

How to cite this article: Lowe RA, Barber KE, Wagner JL, Bell-Harlan AM, Stover KR. Ceftriaxone for the treatment of methicillin-susceptible *Staphylococcus aureus* Bacteremia: A case series. J Pharmacol Pharmacother 2017;8:140-4.

Received: 03-03-2017 **Revised:** 14-06-2017 **Accepted:** 10-07-2017

brain emboli. He was discharged on hospital day 44, and ceftriaxone therapy was continued for 8 additional weeks.

Case 2

A 68-year-old female had positive blood cultures for MSSA and a paraspinal abscess, which was subsequently drained, and a TEE displayed a large vegetation on the right atrial junction. She was initially treated with oxacillin 2 g every 4 h from days 5 to 12. Negative blood cultures were obtained on day 9. On discharge (day 13), ceftriaxone 2 g every 24 h was initiated for completion of 6 weeks of therapy from first negative blood culture. Follow-up computed tomography (CT) scans showed that the paraspinal abscess resolved.

Case 3

A 66-year-old male with PMH including DM and hypertension (HTN) was admitted for septicemia secondary to cellulitis of the left great toe. He received vancomycin until day 3, when blood cultures revealed MSSA. Oxacillin 2 g every 4 h was administered from hospital days 4 through 7, then oxacillin was changed to ceftriaxone 2 g every 24 h for 4 weeks of therapy.

Case 4

A 64-year-old female admitted for shortness of breath, weakness, and fatigue with a PMH of HTN, DM, heart failure, atrial fibrillation, and end-stage renal disease (ESRD) had positive MSSA blood cultures from admission. A definitive source for the MSSA BSI was not determined but assumed to be foreign body material (tunneled dialysis catheter, Foley catheter, and implantable cardiac device). She was initiated on ceftriaxone 2 g every 24 h on day 3 and cultures cleared on day 8. She received 4 weeks of ceftriaxone (25 days inpatient and 3 days outpatient).

Case 5

A 57-year-old male was admitted for sepsis secondary to septic arthritis of the right hip and left shoulder. He had a PMH of rheumatoid arthritis and was receiving long-term immunosuppressive therapy with prednisone. Blood cultures on admission were positive for MSSA. On day 3, the left shoulder was irrigated and debrided. Ceftriaxone 2 g every 24 h was initiated on day 6 for 6 weeks of therapy from first negative blood culture. An MRI revealed erosive changes along both sides of the right hip joint, and an antibiotic spacer was placed on hospital day 7.

Case 6

A 55-year-old male was admitted with severe pain secondary to a fall with a PMH for HTN and advanced alcoholic cirrhosis. Blood cultures on day 1 were positive for MSSA. Oxacillin 2 g every 4 h was given on days 3–12. The patient achieved MC but failed to achieve CC (WBCs did not normalize within 7 days). On discharge (day 12), he was switched from oxacillin to ceftriaxone 2 g every 24 h. The patient died from liver disease complications 7 days after discharge.

Case 7

A 49-year-old male was admitted for symptoms of an upper respiratory tract infection with a nonhealing diabetic foot wound secondary to longstanding DM with diabetic neuropathy and HTN. Blood cultures revealed MSSA on day 1, and ceftriaxone 2 g every 24 h was initiated on day 2 with clearance observed on day 3. X-rays suggested osteomyelitis, and a below the knee amputation was performed on day 5. Postamputation, ceftriaxone 2 g every 24 h was continued for 4 weeks. The patient was readmitted twice the following month, once for a fall that caused bleeding at the site of the amputation and once for debridement, but cultures did not reveal any MSSA, and no MSSA BSI-related recurrence was noted on either admission.

Case 8

A 47-year-old male admitted for MSSA septicemia secondary to a laceration repair on the back of the head 9 days prior had positive surgical site and blood cultures with MSSA. Oxacillin 2 g every 4 h was initiated on day 4. Echocardiogram was negative for vegetations, and on day 11, antimicrobial therapy was switched to ceftriaxone 2 g every 24 h for 6 weeks of therapy.

Case 9

A 41-year-old male with PMH of uncontrolled DM was admitted for cellulitis of the left lower leg. He continued to worsen despite 5 days of outpatient therapy with clindamycin. Foot ulcer and blood cultures from hospital day 1 grew MSSA; MRI was not indicative of osteomyelitis or septic arthritis. Clindamycin was discontinued, and oxacillin 2 g every 4 h was initiated on day 5. On day 7, oxacillin was changed to ceftriaxone 2 g every 24 h for 4 weeks of outpatient therapy.

Case 10

A 40-year-old female admitted for a BSI with an abscess on her left arm was hospitalized 2 days prior for new-onset DM. Blood cultures drawn on the day of discharge from the previous hospitalization grew MSSA. New blood cultures were obtained, and she was initiated on vancomycin therapy. On day 2, cultures revealed MSSA; vancomycin was discontinued, and oxacillin 2 g every 4 h was prescribed. On day 5, oxacillin was discontinued and she was discharged with ceftriaxone 2 g every 24 h to complete 4 weeks of therapy.

Case 11

A 36-year-old female was admitted for diabetic ketoacidosis (DKA), sepsis, right hand cellulitis, and a right patellar fracture. Her PMH included ESRD, DM, and diabetic nephropathy. She was treated for DKA in the intensive care unit, and her dialysis port was removed as a source of infection. Dialysis port cultures and blood cultures revealed MSSA. She was initially treated with vancomycin, which was de-escalated to oxacillin for days 5 through 9. Oxacillin was switched to cefazolin 2 g every 48 h for days 10 through 13, then changed to ceftriaxone 2 g every 24 h on day 14. She was discharged home on day 21 with 4 weeks of outpatient ceftriaxone.

Case 12

A 35-year-old female with PMH of invasive breast carcinoma with reported tenderness around her chemotherapy port for

1 week was admitted for Gram-positive BSI. The chemotherapy port was removed on day 2 and cultured MSSA. Vancomycin was discontinued in favor of oxacillin 2 g every 4 h until day 5, when oxacillin was discontinued, and she was discharged on 2 weeks of ceftriaxone 2 g every 24 h.

Case 13

A 35-year-old female was admitted for fever with swelling and pain at the site of the peripherally inserted central catheter (PICC) in her left arm. She had a PMH of gastroparesis with multiple abdominal surgeries and was reliant on total parenteral nutrition. Blood cultures revealed MSSA, and her PICC was removed for 48 h before a new one was placed. She received ceftriaxone 1 g every 24 h on days 1–3. Ceftriaxone was switched to oxacillin 2 g every 6 h on day 4. She was changed back to ceftriaxone 2 g every 24 h on day 12, then discharged to a long-term acute care (LTAC) facility on day 23. She continued ceftriaxone at LTAC for 8 additional days.

Case 14

A 24-year-old male with PMH of testicular cancer and recent chemotherapy was admitted from an OSH with fever and given cefepime. On day 2, blood and sputum cultures became positive for MSSA, and cefepime was de-escalated to oxacillin 2 g every 4 h. A chest CT displayed cavitary lesions determined to be caused by MSSA. It was suspected that the MSSA BSI was due to septic emboli from a central line infection, and his chemotherapy port was removed. On day 8, oxacillin was discontinued, and he was initiated on ceftriaxone 2 g every 24 h. He was discharged on day 10 to complete 4 weeks of therapy. Nine days after discharge, he was readmitted with progressive shortness of breath, fever, chills, and night sweats. A pleural fluid culture yielded MSSA, so he received ceftriaxone on days 1–4 and oxacillin on days 4–7. He was discharged on ceftriaxone therapy to complete the 4 weeks.

Case 15

A 19-year-old male admitted for possible meningitis presented with numbness and fever and developed acute paraplegia secondary to a spinal abscess. Surgical and blood cultures revealed MSSA on day 1, then the patient developed sepsis secondary to a pulmonary septic embolus. Vancomycin was discontinued, and oxacillin 2 g every 4 h was initiated on day 4. He had negative blood cultures on day 6. On day 14, he was discharged to rehabilitation on ceftriaxone 2 g every 24 h for 8 weeks.

Discussion

We described the successful use of ceftriaxone for MSSA BSI [Table 1]. Of the 15 cases presented, four received ceftriaxone therapy on MSSA identification, whereas 11 received SOCT first. All ceftriaxone-treated patients empirically received vancomycin for 2.5 ± 1.7 days and achieved MC with a duration of bacteremia of 6.8 ± 5.2 days. However, only 75% achieved CC. A CC was not observed in case #1 due to prolonged bacteremia (14 days) though this is likely attributed to inadequate source control. Of the 11 patients treated with SOCT first, 10 received vancomycin therapy for 2.6 ± 1.0 days before initiation of SOCT, and all 11 received SOCT for 6.1 ± 3.0 days before ceftriaxone. All achieved MC, but only 5/11 (45.5%) demonstrated CC. Of CC failures, 5 (86%) had prolonged elevation of WBC. Ceftriaxone was started on the majority (81.8%) of these patients post bloodstream clearance. These data demonstrate ceftriaxone may be an appropriate agent once bacteremia is resolved, particularly in an outpatient setting [Table 2]. This is supported by only a single case of MSSA readmittance.

These cases demonstrated similar ceftriaxone cure rates as previously published literature.[7] While only four

Table 1: Summary of patient cases

Patient case	Infection source	Treatment	Clinical cure?	Microbiological cure?	LOS (days)	MSSA BSI-related readmission?
1	UTI	CRO	No	Yes	44	No
2	IE	SOCT→CRO	No	Yes	13	No
3	SSTI	SOCT→CRO	Yes	Yes	7	No
4	Prosthetic device	CRO	Yes	Yes	28	No
5	Septic arthritis	CRO	Yes	Yes	13	No
6	Unspecified	SOCT→CRO	No	Yes	23	No
7	Osteomyelitis	CRO	No	Yes	13	No
8	Surgical site	SOCT→CRO	No	Yes	12	No
9	SSTI	SOCT→CRO	No	Yes	9	No
10	Central line	SOCT→CRO	Yes	Yes	5	No
11	Dialysis port	SOCT→CRO	No	Yes	21	No
12	Chemo port	SOCT→CRO	Yes	Yes	5	No
13	Central line	SOCT→CRO	Yes	Yes	23	No
14	Pneumonia	SOCT→CRO	Yes	Yes	10	Yes
15	CNS	SOCT→CRO	No	Yes	14	No

LOS=Length of stay, MSSA=Methicillin-susceptible *Staphylococcus aureus*, BSI=Bloodstream infection, UTI=Urinary tract infection, IE=Infective endocarditis, CRO=Ceftriaxone, SOCT=Standard of care therapy, SSTI=Skin and soft tissue infections, CNS=Central nervous system

Table 2: Comparison of treatment durations in days

Patient case	Total duration of antibiotic therapy	Duration of initial SOCT therapy	Corrected total duration of CRO therapy	Duration of CRO therapy inpatient	Duration of CRO therapy outpatient
1	100	0	100	41	56
2	50	8	42	0	42
3	32	4	28	0	28
4	28	0	28	25	3
5	42	0	42	6	36
6	17	10	7	0	7
7	28	0	28	12	16
8	50	8	42	1	41
9	31	3	28	0	28
10	32	4	28	0	28
11	45	9	36	8	28
12	15	3	12	0	12
13	32	9	23	15	8
14	28	7	21	3	18
15	67	11	56	0	56

SOCT=Standard of care therapy, CRO=Ceftriaxone

patients received ceftriaxone initially, clinical success was 75% compared to 83% in the Patel *et al*. study. However, our series represented a more diverse and younger population (60% males, average age 47 years) compared to a VA Institution (100% males, average age 68 [SOCT] and 63 [ceftriaxone] years).[11]Another evaluation comparing ceftriaxone versus cefazolin demonstrated similar duration of SOCT therapy before initiation of ceftriaxone.[12] However, neither the source of BSI nor specific outcomes of each antimicrobial were reported. Unlike a study comparing ceftriaxone versus nafcillin for outpatient parenteral therapy against MSSA,[13] no adverse events were observed in any of our patients.

However, higher rates of treatment failure with ceftriaxone versus cefazolin for MSSA bacteremia, including a possible increased mortality, have been observed.[11,14] Of note, one study included high-acuity patients and failed to state whether patients received adequate duration of treatment with ceftriaxone before treatment failure was declared.[11] The second study declared ceftriaxone to have higher mortality rates but was not considered statistically significant, and no other outcomes were measured.[14]

This case series provides vital data to support ceftriaxone for treatment of MSSA BSI. The majority of patients received SOCT before ceftriaxone therapy, so while the CC and MC may be attributed to SOCT, it is important to note that these infections require prolonged courses of therapy. Therefore, the few recurrences of infection demonstrate that ceftriaxone was an effective option for maintenance therapy after resolution of the BSI.

Acknowledgments

This case series was presented in part at Infectious Diseases Week 2016 in New Orleans, Louisiana on October 28th, 2016.

All named authors meet the International Committee of Medical Journal Editors criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval to the version to be published.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Laupland KB. Incidence of bloodstream infection: A review of population-based studies. Clin Microbiol Infect 2013;19:492-500.
2. Laupland KB, Lyytikäinen O, Søgaard M, Kennedy KJ, Knudsen JD, Ostergaard C, *et al*. The changing epidemiology of *Staphylococcus aureus* bloodstream infection: A multinational population-based surveillance study. Clin Microbiol Infect 2013;19:465-71.
3. Tom S, Galbraith JC, Valiquette L, Jacobsson G, Collignon P, Schønheyder HC, *et al*. Case fatality ratio and mortality rate trends of community-onset *Staphylococcus aureus* bacteraemia. Clin Microbiol Infect 2014;20:O630-2.
4. Youngster I, Shenoy ES, Hooper DC, Nelson SB. Comparative evaluation of the tolerability of cefazolin and nafcillin for treatment of methicillin-susceptible *Staphylococcus aureus* infections in the outpatient setting. Clin Infect Dis 2014;59:369-75.
5. Lee S, Choe PG, Song KH, Park SW, Kim HB, Kim NJ, *et al*. Is cefazolin inferior to nafcillin for treatment of methicillin-susceptible *Staphylococcus aureus* bacteremia? Antimicrob Agents Chemother 2011;55:5122-6.
6. Housman ST, Sutherland CA, Nicolau DP. Pharmacodynamic profile of commonly utilised parenteral therapies against meticillin-susceptible and meticillin-resistant *Staphylococcus aureus* collected from US hospitals. Int J Antimicrob Agents 2014;44:235-41.
7. Patel UC, McKissic EL, Kasper D, Lentino JR, Pachucki CT, Lee T, *et al*. Outcomes of ceftriaxone use compared to standard of therapy in methicillin susceptible *Staphylococcal aureus* (MSSA) bloodstream infections. Int J Clin Pharm 2014;36:1282-9.
8. Phe K, Dao D, Palmer HR, Tam VH. *In vitro* ceftriaxone susceptibility in methicillin-susceptible *Staphylococcus aureus*. Antimicrob Agents Chemother 2015;59:1370.

9. Kang N, Housman ST, Nicolau DP. Assessing the surrogate susceptibility of oxacillin and cefoxitin for commonly utilized parenteral agents against methicillin-susceptible *Staphylococcus aureus*: Focus on ceftriaxone discordance between predictive susceptibility and *in vivo* exposures. Pathogens 2015;4:599-605.
10. Jones RN, Sader HS, Fritsche TR, Pottumarthy S. Comparisons of parenteral broad-spectrum cephalosporins tested against bacterial isolates from pediatric patients: Report from the SENTRY Antimicrobial Surveillance Program (1998-2004). Diagn Microbiol Infect Dis 2007;57:109-16.
11. Carr D, Bonomo RA, Stiefel U, Sims S. Cefazolin versus ceftriaxone for the treatment of methicillin-susceptible *Staphylococcus aureus* bacteremia in a tertiary-care veterans affairs medical center. Open Forum Infect Dis 2015;2:1-66.
12. Winans SA, Luce AM, Hasbun R. Outpatient parenteral antimicrobial therapy for the treatment of methicillin-susceptible *Staphylococcus aureus*: A comparison of cefazolin and ceftriaxone. Infection 2013;41:769-74.
13. Wynn M, Dalovisio JR, Tice AD, Jiang X. Evaluation of the efficacy and safety of outpatient parenteral antimicrobial therapy for infections with methicillin-sensitive *Staphylococcus aureus*. South Med J 2005;98:590-5.
14. Paul M, Zemer-Wassercug N, Talker O, Lishtzinsky Y, Lev B, Samra Z, *et al.* Are all beta-lactams similarly effective in the treatment of methicillin-sensitive *Staphylococcus aureus* bacteraemia? Clin Microbiol Infect 2011;17:1581-6.