

A Retrospective Comparison of Ceftriaxone Versus Oxacillin for Osteoarticular Infections Due to Methicillin-Susceptible *Staphylococcus aureus*

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Background. Antistaphylococcal penicillins are the treatment of choice for methicillin-susceptible *Staphylococcus aureus* (MSSA) infection. Ceftriaxone can be dosed once daily and is less expensive for outpatient therapy than oxacillin. We compared patient outcomes of MSSA osteoarticular infections treated with ceftriaxone versus oxacillin.

Methods. We conducted a retrospective cohort study of patients with MSSA osteoarticular infections at a tertiary care hospital from January 2005 to April 2010. We collected demographic, clinical, and outcome data including treatment-related adverse events. Successful treatment (clinical improvement; improved follow-up markers and imaging; no readmission for treatment) was compared at 3–6 months and >6 months after completion of intravenous antibiotics.

Results. In total, 124 patients had an MSSA osteoarticular infection; 64 (52%) had orthopedic hardware involvement. Of those patients, 74 (60%) received ceftriaxone and 50 (40%) received oxacillin. Oxacillin was more often discontinued due to toxicity (9 of 50 [18%] oxacillin vs 3 of 74 [4%] ceftriaxone; $P = .01$). At 3–6 months, data for 97 and 88 patients, respectively, were available for analysis. Treatment success was similar at 3–6 months (50 of 60 [83%] ceftriaxone vs 32 of 37 [86%] oxacillin; $P = .7$) and >6 months (43 of 56 [77%] ceftriaxone vs 26 of 32 [81%] oxacillin; $P = .6$). After intravenous antibiotics, 56 (45%) patients received long-term suppression with oral antibiotics (31 of 74 [42%] ceftriaxone vs 25 of 50 [50%] oxacillin; $P = .4$).

Conclusions. In this comparison of ceftriaxone versus oxacillin for MSSA osteoarticular infections, there was no difference in treatment success at 3–6 and >6 months following the completion of intravenous antibiotics. Patients receiving oxacillin were more likely to have it discontinued due to toxicity.

Staphylococcus aureus is the most frequent organism isolated in osteoarticular infections [1]. The treatment options for *S. aureus* infections depend on the resistance pattern of the isolate. For methicillin-sensitive *S. aureus* (MSSA) infections, the drugs of choice are the antistaphylococcal penicillins (oxacillin, nafcillin, and

methicillin) [2]. Few studies have compared the standard antistaphylococcal penicillins to newer β -lactam antibiotics such as cephalosporins. Ceftriaxone, a third-generation, long-acting, intravenous cephalosporin, has been shown to be an effective treatment for MSSA infections in general [3, 4]. There are limited data supporting the use of ceftriaxone for the treatment of osteoarticular infections due to MSSA [5], although its bone penetration is similar to that of penicillins [6]. Ceftriaxone is attractive for treatment of bone and joint infections for a number of reasons. It is well tolerated [7] and given once daily, whereas oxacillin is given either 6 times per day or via continuous infusion. Once-daily dosing may improve patients' adherence to outpatient antibiotic therapy [8]. Also, it is

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comparatively inexpensive [9]. Because osteoarticular infections require prolonged intravenous treatment courses of at least 4–6 weeks, tolerability, convenience, and cost are important considerations in the antibiotic choice [10]. To our knowledge, there has never been a direct comparison of clinical outcomes in MSSA osteoarticular infections treated with ceftriaxone versus antistaphylococcal penicillins. Our study sought to retrospectively compare treatment outcomes of MSSA osteoarticular infections treated with ceftriaxone versus oxacillin at our institution. We hypothesized that rates of clinical treatment success after 3 and 6 months following the completion of intravenous antibiotics would be similar irrespective of the treatment group. A secondary goal was to compare the tolerability of the 2 medications and the frequency of treatment modifications due to antibiotic toxicity.

METHODS

Study Design and Population

This retrospective cohort study was conducted at Barnes-Jewish Hospital, a 1250-bed tertiary care hospital in St Louis, Missouri. Patients diagnosed with MSSA osteomyelitis and/or septic arthritis who were treated with either intravenous ceftriaxone or oxacillin were identified through the Washington University Infectious Diseases Division outpatient antibiotic therapy database. The inclusion criteria for this study were the following: (1) age ≥ 18 years, (2) admission to the hospital between 1 January 2005 and 30 April 2010, and (3) diagnosis of MSSA osteomyelitis and/or septic arthritis with a culture from bone, deep tissue, and/or joint fluid. Patients were excluded for the following criteria: (1) prior osteoarticular infection with MSSA, (2) confirmed polymicrobial infection, or (3) treatment with multiple antibiotics for assumed polymicrobial infection.

Clinical Data Collection

Data on included subjects were collected through review of their inpatient and outpatient electronic medical records using a standardized data collection tool. Clinical data collected consisted of demographic characteristics, patient comorbidities, pertinent medications including immunosuppressive therapy, clinical presentation, diagnostic workup (including laboratory results, microbiology results, and imaging studies), and the type and planned duration of antibiotic treatment. Data obtained from the outpatient electronic medical record (including infectious diseases and surgical subspecialty clinics) included signs and symptoms of infection noted during the follow-up visit(s), functional status, documentation of adverse events related to antibiotic administration, laboratory data, imaging studies, and oral suppressive antibiotic recommendations. These data were used to determine whether there was evidence of successful treatment or treatment failure.

The cost of outpatient intravenous antibiotic therapy was estimated based on information from the hospital's home infusion provider. Daily charges were \$160 for ceftriaxone 2 grams administered intravenously every 24 hours (including supplies and excluding home nursing visits), and \$249 for oxacillin 4 grams administered intravenously every 6 hours (including continuous pump [\$16.40 per day] and other supplies, excluding home nursing visits). We projected these charges over the total duration of intravenous antibiotics, regardless of the initial duration of in-hospital treatment.

Definitions

Criteria for successful treatment were defined before data collection. These criteria were applied to findings at follow-up visits after the completion of the intravenous antibiotic course. Visits between 3 and 6 months after intravenous antibiotic completion were considered early follow-up; visits >6 months after intravenous antibiotic completion were considered late follow-up [11].

There is no uniformly used definition in the literature for treatment success in osteoarticular infections [12]. We modified a previously used definition [5]:

1. Resolution of signs and symptoms of infection and
2. Improvement of function and
3. Improvement of inflammatory markers and/or follow-up imaging (when available) and
4. No repeat surgery or readmission for treatment related to the bone or joint infection.

Renal insufficiency was defined as a serum creatinine level ≥ 2 mg/dL or history of dialysis. Immunosuppression was defined as medication with corticosteroids (≥ 10 mg of prednisone equivalent per day) or other immunosuppressants, including being on chemotherapy at time of inclusion. Laboratory parameters of interest and their acceptable ranges were white blood cell count (3.8–9.8 K/mm^3), serum creatinine (< 2 mg/dL), aspartate aminotransferase (11–47 U/L), and alanine aminotransferase (7–53 U/L). Hemoglobin and platelet count were also monitored, but no patient developed new or worsening anemia or thrombocytopenia during the study. Oral suppressive antibiotics were defined as antibiotics directed at MSSA that were given after completion of the intravenous antibiotic course.

Statistical Analysis

Statistical analysis was performed using SPSS software, version 18 (IBM SPSS, Chicago, Illinois). The primary end point was successful treatment at early and late follow-up visits. Secondary end points were tolerability of antibiotic treatment and estimated cost of the intravenous antibiotic course. We used χ^2 test or Fisher exact test for categorical variables, and t test or Mann-Whitney U test for continuous variables as appropriate. A 2-sided P value of $< .05$ was considered statistically significant.

We developed a propensity score for ceftriaxone treatment by balancing potential confounders across the treatment groups in a nonparsimonious approach. The propensity score (PS) was inversely weighted for ceftriaxone ($1/PS$) and oxacillin ($1/(1 - PS)$), respectively [13, 14]. For this analysis, SAS software, version 9.2 (SAS Institute Cary, North Carolina) was used. We constructed regression models for treatment success at early and late follow-up, including the treatment group and weighting by the inverse probability of treatment.

The study was approved by the Washington University Human Research Protection Office.

RESULTS

During the 64-month study period we identified 124 patients in the Infectious Diseases Division outpatient antibiotic therapy databases who were treated for MSSA osteoarticular infections with either ceftriaxone or oxacillin. Of these 124 patients, 74 patients (60%) were treated with ceftriaxone and 50 (40%) were treated with oxacillin (Table 1). The mean age was 52 years ($SD \pm 16$ years). Patients were predominantly male (60%) and white (79%). Comorbidities like diabetes mellitus (24 [19%]), rheumatoid arthritis (10 [8%]), and a concurrent malignancy (4 [3%]) were infrequent. Thirteen patients (11%) were undergoing some form of medical immunosuppression (corticosteroids, immunomodulators, or chemotherapy).

Of the 124 patients, 90 were diagnosed with osteomyelitis (73%), 57 with septic arthritis (46%), and 23 (19%) with both. A total of 88 (71%) infections were due to contiguous spread, whereas 36 (29%) were hematogenous. Most contiguous infections were considered postoperative (71 [57%]); fewer infections were related to a soft tissue ulcer (9 [7%]) or trauma (5 [4%]). Sixty-four patients (52%) had orthopedic hardware in place at the site of infection at the time of index hospital admission. One hundred ten patients (89%) were discharged home from their index hospital admission, and 14 (11%) were transferred to a nursing home or rehabilitation facility.

Comparison of Treatment Groups

Baseline characteristics were similar between the 2 treatment groups (Table 1). Similar percentages of patients in both groups were diagnosed with septic arthritis and osteomyelitis. Orthopedic hardware was present in 43 patients (58%) treated with ceftriaxone and 21 patients (42%) treated with oxacillin ($P = .08$). Patients with fever (14 [19%] vs 2 [4%]; $P = .030$), peripheral vascular disease (8 [11%] vs 0 [0%]; $P = .02$), and penicillin allergy (10 [14%] vs 1 [2%]; $P = .05$) were more likely to be treated with ceftriaxone. Among laboratory tests on admission, platelets were found to be significantly higher in the oxacillin group ($P = .002$). The erythrocyte sedimentation rate was higher at baseline in patients treated with oxacillin

($P = .03$). There were no differences in white blood cell count or C-reactive protein on admission (Table 1).

The majority of patients underwent incision and debridement (62 [84%] ceftriaxone vs 40 [80%] oxacillin; $P = .6$). Among 64 patients with orthopedic hardware in place, the surgical team elected to either leave hardware in place (11 of 43 [26%] ceftriaxone vs 2 of 21 [9%] oxacillin; $P = .2$) or perform total hardware explantation (16 of 43 [37%] ceftriaxone vs 8 of 21 [38%] oxacillin; $P = .9$) or partial explantation (9 of 43 [21%] ceftriaxone vs 4 of 21 [19%] oxacillin; $P > .99$) in similar proportions of both treatment groups. New hardware was inserted in 8 patients (11%) in the ceftriaxone group versus 4 patients (8%) in the oxacillin group ($P = .8$).

Evaluation of Treatment Outcomes

Overall, the median duration of intravenous antibiotics was 43 days (range, 22–132), without a significant difference between the treatment groups (42 days [range, 27–132] in the ceftriaxone group vs 46 days [range, 22–85] in the oxacillin group; $P = .3$). A similar proportion of patients were treated with adjuvant oral rifampin (600–900 mg per day) in each group (15 [20%] ceftriaxone vs 8 [16%] oxacillin; $P = .5$). Thirty-four patients (46%) in the ceftriaxone group and 16 patients (32%) in the oxacillin group left the hospital with hardware in situ ($P = .1$). After completing the intravenous antibiotic course, 56 patients (45%) received oral suppression (31 of 74 patients [42%] vs 25 of 50 patients [50%]; $P = .4$). The most frequently used oral antibiotics were trimethoprim/sulfamethoxazole (34 patients [61%]), doxycycline (8 patients [14%]), and clindamycin (3 patients [5%]). Doxycycline was given more frequently after ceftriaxone (8 [11%] vs 0 [0%]; $P = .02$).

Two patients were lost to follow-up before completing intravenous antibiotics and could not be evaluated regarding outcomes. For the 122 evaluable patients at the time of intravenous antibiotic completion, 97 patients had data at 3–6-month follow-up visits, and 88 patients had data available for follow-up visits >6 months after completing intravenous antibiotics (median, 6.5 months). There was no difference in the proportion of patients lost to follow-up between the treatment groups at the earlier (14 [19%] ceftriaxone vs 13 [26%] oxacillin; $P = .3$) and later clinic visits (18 [24%] ceftriaxone vs 18 [36%] oxacillin; $P = .2$). Treatment success was similar between groups at the 3–6-month follow-up (50 of 60 [83%] ceftriaxone vs 32 of 37 [86%] oxacillin; $P = .7$) and at the >6-month follow-up (43 of 56 [77%] ceftriaxone vs 26 of 32 [81%] oxacillin; $P = .6$).

The effect of treatment group assignment on outcomes was weighted by the propensity score for being administered ceftriaxone. There was no association between treatment group and outcomes at early follow-up (odds ratio [OR], 1.2 [95% confidence interval {CI}, .7–2.1]) or late follow-up (OR, 1.1 [95% CI, .6–1.9]).

Table 1. Characteristics of 124 Patients With Osteoarticular Infections Due to Methicillin-Susceptible *Staphylococcus aureus*

Characteristic	Total (N = 124)	Ceftriaxone (n = 74)	Oxacillin (n = 50)	P value
Age, years, mean (\pm SD)	51.6 (\pm 15.9)	51.1 (\pm 17.7)	52.4 (\pm 12.7)	.6
Sex, male	74 (60%)	44 (60%)	30 (60%)	>.99
Race, white	98 (79%)	62 (84%)	36 (72%)	.1
BMI, kg/cm ² , mean (range)	27 (17–58)	28 (20–58)	27 (17–48)	.2
Antibiotic allergy (any)	27 (22%)	20 (27%)	7 (14%)	.09
Penicillin allergy	11 (9%)	10 (14%)	1 (2%)	.05
Prior osteoarticular infection	30 (24%)	19 (26%)	11 (22%)	.6
Diabetes mellitus	24 (19%)	16 (22%)	8 (16%)	.4
Rheumatoid arthritis	10 (8%)	4 (5%)	6 (12%)	.2
Peripheral vascular disease	8 (7%)	8 (11%)	0	.02
Degenerative joint disease	23 (19%)	12 (16%)	11 (22%)	.4
Renal insufficiency	3 (2%)	2 (3%)	1 (2%)	>.99
HIV infection	1 (1%)	0	1 (2%)	.4
Current cancer	4 (3%)	2 (3%)	2 (4%)	>.99
Immunosuppression (steroids, immunomodulators, chemotherapy)	13 (11%)	5 (7%)	8 (16%)	.1
Current or former smoker	45 (36%)	31 (42%)	14 (28%)	.1
Orthopedic hardware on admission	64 (52%)	43 (58%)	21 (42%)	.08
Osteomyelitis	90 (73%)	51 (69%)	39 (78%)	.3
Septic arthritis	57 (46%)	33 (45%)	24 (48%)	.7
Fever on admission (>38.3°C)	16 (13%)	14 (19%)	2 (4%)	.03
Diagnostic indicators on admission				
Blood cultures drawn	67 (54%)	36 (49%)	31 (62%)	.1
\geq 1 positive blood culture for MSSA	25/67 (37%)	12/36 (33%)	13/31 (42%)	.5
Radiography consistent with bone or joint infection	43/96 (45%)	25/57 (44%)	18/39 (46%)	.8
CT scan consistent with bone or joint infection	23/33 (73%)	11/14 (79%)	13/19 (68%)	.5
MRI consistent with bone or joint infection	26/29 (90%)	12/15 (80%)	14/14 (100%)	.2
Bone scan consistent with bone or joint infection	7/9 (78%)	3/5 (60%)	4/4 (100%)	.4
White blood cell count, K/mm ³ , median (range)	10.4 (2.7–27.1)	9.3 (2.7–25.2)	10.6 (4.4–27.1)	.3
Platelets, K/mm ³ , median (range)	299 (14–1755)	274 (14–1755)	362 (113–749)	.002
Serum creatinine, mg/dL, median (range)	0.9 (0.5–9.0)	0.9 (0.5–9.0)	0.9 (0.5–4.3)	.2
ESR, mm/h, median (range)	65 (2–140)	55 (2–140)	82 (12–140)	.03
CRP, mg/L, median (range)	72 (0.2–445)	60 (0.2–307)	116 (0.8–445)	.07
Serum glucose, mg/dL, median (range)	112 (51–299)	114 (51–299)	107 (70–199)	.3
Any surgical treatment	110 (89%)	67 (91%)	43 (86%)	.4
Outcomes				
Treatment successful at 3–6 months follow-up	82/97 (85%)	50/60 (83%)	32/37 (86%)	.7
Subset of osteomyelitis	41/47 (87%)	26/30 (87%)	15/17 (88%)	>.99
Subset of septic arthritis	26/30 (87%)	18/22 (82%)	8/8 (100%)	.6
Treatment successful at >6 months follow-up	69/88 (78%)	43/56 (77%)	26/32 (81%)	.6
Subset of osteomyelitis	36/43 (84%)	24/29 (83%)	12/14 (86%)	>.99
Subset of septic arthritis	22/28 (79%)	15/20 (75%)	7/8 (88%)	.6

All values expressed as no. (%), unless otherwise indicated. Mixed septic arthritis and osteomyelitis infections were not considered in the comparison of subsets. Abbreviations: BMI, body mass index; CRP, C-reactive protein; CT, computed tomography; ESR, erythrocyte sedimentation rate; HIV, human immunodeficiency virus; MRI, magnetic resonance imaging; MSSA, methicillin-susceptible *Staphylococcus aureus*; SD, standard deviation.

In patients admitted with hardware-associated infections, treatment success was similar across the treatment groups at early (30 of 37 [81%] ceftriaxone vs 14 of 15 [93%] oxacillin; $P = .4$) and late follow-up (25 of 34 [74%] ceftriaxone vs 11 of 13 [85%] oxacillin; $P = .7$). Findings in those discharged with hardware in place were similar at early (treatment success in

22 of 29 [76%] ceftriaxone vs 14 of 14 [100%] oxacillin; $P = .08$) and late follow-up (20 of 29 [69%] ceftriaxone vs 11 of 12 [92%] oxacillin; $P = .2$). In patients with hardware in place at discharge, similar proportions were given oral suppressive antibiotics (23 of 34 [68%] ceftriaxone vs 11 of 16 [69%] oxacillin; $P = .9$). Patients who were given concomitant rifampin had

similar success rates in both treatment groups at early ($P = .09$) and late follow-up ($P = .09$).

Complications of Outpatient Antibiotic Treatment

Ceftriaxone was less frequently discontinued due to toxicity compared with oxacillin (3 of 74 [4%] vs 9 of 50 [18%], respectively; $P = .01$). Two patients in each group had antibiotics changed due to allergic reactions ($P > .99$). There was 1 (1%) catheter-associated infection in the ceftriaxone group versus 2 (4%) in the oxacillin group ($P = .6$); the patient in the ceftriaxone group was switched to oral antibiotics after the catheter infection. A single case of *Clostridium difficile*-associated diarrhea occurred in the ceftriaxone group.

Abnormal laboratory values were reported in 5 patients (7%) receiving ceftriaxone and in 11 patients (22%) receiving oxacillin ($P = .01$). A total of 9 patients had elevated liver function tests (1 in the ceftriaxone group and 8 in the oxacillin group); these abnormalities prompted a change in antibiotics in 7 of 8 patients on oxacillin. Five patients developed neutropenia, of whom 1 patient in each group was changed to another antibiotic due to this adverse event. There was no association between age or baseline serum creatinine level and the occurrence of drug-related toxicity (data not shown).

The median cost estimate per intravenous antibiotic treatment course was projected based on standard daily expense and was significantly lower in the ceftriaxone group (\$6720 [range, \$4320–\$21 120] vs \$11 329 [range, \$5478–\$21 165]; $P < .001$).

DISCUSSION

There are few well-designed, adequately powered randomized controlled trials to compare various antibiotics in the treatment of osteoarticular infections [15]. Accordingly, practices vary greatly and often rely on individual experience and prescriber preference. The standard treatment of osteoarticular infections due to MSSA, for example, are penicillinase-resistant penicillins like oxacillin and nafcillin [1]. At our institution, ceftriaxone is increasingly being used for treating this common cause of bone and joint infections. Our practice is derived from a single case series of 22 osteoarticular MSSA infections that documented favorable treatment outcomes with ceftriaxone [5] and is driven by practical implications of outpatient treatment [16].

Outpatient parenteral antibiotic therapy (OPAT) is commonly used for infections that require prolonged antibiotic courses. It has been postulated that ease of administration improves adherence to outpatient intravenous antibiotics [8]. Ceftriaxone is relatively easy to administer and has a low phlebitis risk and a favorable safety profile. Although there are earlier reports of ceftriaxone being labile in the presence of large bacterial inocula, a more recent study has not confirmed this [17].

In our study, overall treatment success was similar at early and late follow-up visits, with 85% and 78% success rates, respectively.

There was also no significant difference in treatment success between the 2 study drugs, ceftriaxone and oxacillin; our findings therefore support the use of ceftriaxone in outpatient antibiotic therapy for osteoarticular infections. Randomized controlled trials have shown ceftriaxone to be as effective as an alternative; however, these studies used cefotaxime and ampicillin/sulbactam as comparators and included only small subsets of osteoarticular infections [18, 19]. A case series by Guglielmo et al [5] reported a 77% success rate with ceftriaxone, similar to our results, even though they used an additional category of “indeterminate outcome” for patients maintained on oral suppressive antibiotics. There was no comparator group in their study. In a more recent study of OPAT patients with MSSA infection, the authors found similar rates of clinical success in osteoarticular infections treated with ceftriaxone or oxacillin (98% and 92%, respectively). However, clinical success was determined only on the last day of intravenous antibiotics [3]. Other limitations of this study are the lack of information on drug dosages, treatment duration, concomitant oral rifampin use, and subsequent oral suppressive antibiotic use. Also, no information was given on surgical treatment. Another retrospective study examined outcomes of patients treated with OPAT and included 237 patients with MSSA osteomyelitis who had been followed for at least 6 months. They reported that the infection recurrence rate was similar in patients treated with penicillinase-resistant penicillins (28.6%) and ceftriaxone (27.3%) [20]. The duration of treatment was not compared across groups, however, nor was the need for surgery, hardware removal, concomitant medication with rifampin, or subsequent oral antibiotics. Also, this study included patients treated with ceftazolin and vancomycin, and the number of patients treated with ceftriaxone was not disclosed. None of these observational studies compared patient characteristics between different groups to assess for selection bias. Our findings support the role of ceftriaxone in the treatment of MSSA osteoarticular infections by providing the first direct comparison with the standard, oxacillin.

We noted that oxacillin was more frequently discontinued due to toxicity compared with ceftriaxone, most often due to elevated aminotransferases. Wynn et al [3] reported that nafcillin, another antistaphylococcal penicillin, also had a higher rate of adverse events versus ceftriaxone (5.4% vs 1.6%, respectively).

By our estimation of the overall cost of treatment, ceftriaxone was significantly less expensive than oxacillin. This did not take into account hospital and nursing expenses, or costs for laboratory monitoring, but was limited to medication and supplies [21]. Previous analyses have demonstrated that an OPAT program can reduce healthcare costs [22]. Costs can be decreased further if less expensive, equally effective antibiotics are chosen [8].

There are several limitations to this study. This was a comparatively small, single-center, retrospective study. Due to the sample size, we were not able to demonstrate noninferiority of

ceftriaxone. Still, our study reflects 2 concurrent treatment practices at our hospital and is therefore consistent with the goals of comparative effectiveness research. We also used a propensity score-weighted analysis to account for possible selection bias. The study includes patients in whom orthopedic hardware was retained and who were continued on oral antibiotic suppression after the discontinuation of intravenous antibiotics. Although this makes it more difficult to ascribe treatment success to a specific intravenous antibiotic, it is common clinical practice and a reflection of the reality of treating bone and joint infections. We compared the rates of patients on oral suppression and the individual antibiotics that were chosen and could not find differences. Follow-up was limited to a minimum of only 6 months, and not all patients could be assessed throughout the planned follow-up observation period. However, most treatment failures or recurrences of osteoarticular infection occur in the first few months after antibiotic completion; therefore, follow-up may not need to be extended beyond 6–12 months [20]. Finally, beyond the immediate benefit to the patient, there is the public health concern that ceftriaxone with its broader coverage than oxacillin could potentially result in increasing antibiotic resistance when overused.

CONCLUSIONS

The results of this study suggest that ceftriaxone is an effective agent for the treatment of osteoarticular MSSA infections and may produce a similar rate of treatment success as the standard oxacillin. Additional studies, possibly including analyses of large administrative data sets or prospective comparisons, should be undertaken to further document the clinical equivalence of this conveniently dosed and well-tolerated third-generation cephalosporin and determine whether clinical cure can be achieved at a lower cost to the healthcare system.

Notes

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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