Comparison of Cefazolin versus Nafcillin for Methicillin-Susceptible *Staphylococcus aureus* Bacteremia with a Deep-Seated Source

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Background

- Historically, anti-staphylococcal penicillins have been the treatment of choice for methicillin-susceptible *Staphylococcus aureus* (MSSA); however, cefazolin may have similar efficacy and several advantages including:[1,2]
  - More convenient dosing regimen
  - Improved tolerability
  - Reduced sodium and volume administration
- Some prescribers remain hesitant to use cefazolin in deep-seated infections due to the potential of an inoculum effect in the setting of a high bacterial burden[3]
- Existing literature includes small numbers of patients with deep-seated infections, and no studies examine MSSA bloodstream infections (BSI) in a population with exclusively deep-seated sources[4,5]

Methods

- Retrospective cohort study involving the Hospital of the University of Pennsylvania and Penn Presbyterian Medical Center
- Microbiology records between March 1, 2017 and October 31, 2019 were reviewed to identify patients with MSSA BSI, and further analysis of the electronic medical record was conducted to determine study eligibility
- **Primary efficacy outcome: composite of treatment failure, 60-day mortality, and 60-day infection relapse; this was assessed using multivariate logistic regression**
- Primary safety outcome: discontinuation of therapy due to adverse drug events; this was assessed with a chi-square test
- Demographic data were compared using descriptive statistics
- It was estimated that 144 patients would be required in each arm to provide 80% power to detect a 15% difference in the primary efficacy outcome.

Table 1. Inclusion and exclusion criteria used to assess potential patients.

Inclusion Criteria	Exclusion Criteria
• One or more bloodstream isolates of MSSA with a deep-seated source (endocarditis, osteomyelitis, septic arthritis, pneumonia, prosthetic material, mediastinitis, or abscess) between March 1, 2017 and October 31, 2019 • Treated with cefazolin or nafcillin as definitive therapy	• Age < 18 years • Polymicrobial bloodstream infection • Central nervous system infection • Received less than 7 days of definitive therapy

Results

Patient Identification

A total of 506 patients with MSSA BSI were identified, and 164 were ultimately included in the analysis.

Table 2. Characteristics of patients treated with cefazolin or nafcillin for MSSA BSI.

Characteristic	Cefazolin (n=141)	Nafcillin (n=23)	*P* value
Male, n (%)	84 (59.6)	15 (65.2)	0.608
Median age, years (IQR)	58 (21)	58 (23)	0.602
Race, % White Black/AA Other/Unknown	 61 (43.3) 66 (46.8) 14 (9.9)	 13 (56.5) 6 (26.1) 4 (17.4)	0.133
Source, %[a] Endocarditis Osteomyelitis Pneumonia Abscess Prosthetic material Septic arthritis Mediastinitis	 37 (26.2) 24 (17.0) 20 (14.2) 22 (15.6) 52 (36.9) 25 (17.7) 3 (2.1)	 11 (47.8) 3 (13.0) 1 (4.3) 3 (13.0) 7 (30.4) 3 (13.0) 2 (8.7)	 0.259
Source control, n (%)	128 (90.8)	20 (86.9)	0.474
Adjunct therapy, n (%)	13 (9.2)	4 (17.4)	0.264
ID consult, n (%)	140 (99.2)	23 (100.0)	1.00

[a]Patients may have more than one source (total of 213 sources).

Outcomes

Table 3. Outcomes for patients treated with cefazolin or nafcillin for MSSA BSI.

Outcome	Cefazolin (n=141)	Nafcillin (n=23)	*P* value
Primary efficacy outcome, n (%)	33 (23.4)	6 (26.1)	0.779
In-hospital mortality, n (%)	6 (4.3)	1 (4.4)	1.00
30-day mortality, n (%)	9 (6.4)	2 (8.7)	0.654
60-day mortality, n (%)	15 (10.6)	4 (17.4)	0.312
90-day mortality, n (%)	21 (14.9)	4 (17.4)	0.757

Table 3. Outcomes for patients treated with cefazolin or nafcillin for MSSA BSI.

Outcome	Cefazolin (n=141)	Nafcillin (n=23)	*P* value
90-day infection-related readmission, n (%)	25 (17.7)	3 (13.0)	0.768
Median duration of bacteremia, days (IQR)	3 (2)	2 (4)	0.764
Median LOS after index positive blood culture, days (IQR)	11 (11)	16 (19)	0.111
ADE on therapy, n (%)	53 (37.6)	19 (82.6)	**<0.0001**
Discontinued due to ADE, n (%)	8 (5.7)	7 (30.4)	**<0.0001**

Multivariate Analysis

- On univariate analysis, both age (OR 1.03, *P*=0.043) and source control (OR 0.35, *P*=0.056) were found to be significantly associated with the primary outcome
- Both age and source control were included in the final multivariate model
- On multivariate analysis, antibiotic selection was not an independent predictor of the primary efficacy outcome (OR 1.26, *P*=0.663)

Discussion and Conclusions

- Cefazolin and nafcillin appear to have similar efficacy against MSSA BSI with deep-seated sources, though it is difficult to make a true comparison of outcomes due to low nafcillin utilization overall
- Nafcillin results in significantly more adverse drug events necessitating a change in therapy
- Cefazolin may be an appropriate, or even preferential, choice in deep-seated MSSA infections
- Analysis is limited by a small sample size and insufficient power to detect a difference in the primary outcome
- This investigation would be strengthened by additional information regarding underlying comorbidities of the study population, as these likely have implications in overall outcomes

References

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