Penicillin Versus Cefazolin or Anti-staphylococcal Penicillins for Penicillin-Susceptible *Staphylococcus aureus* Bacteremia

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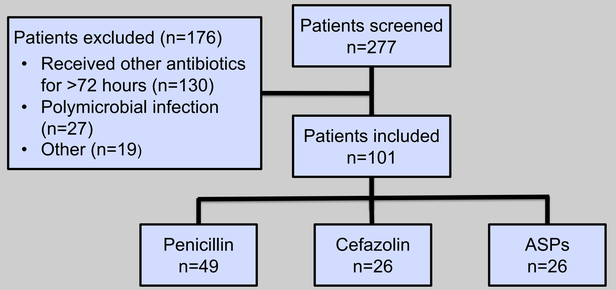
Background

- Methicillin-susceptible *Staphylococcus aureus* (MSSA) bacteremia is a significant cause of mortality[1]
- Recent studies have demonstrated that cefazolin may be non-inferior to the anti-staphylococcal penicillins (ASPs), oxacillin and nafcillin, in the treatment of MSSA, but cefazolin has a broader spectrum of activity[2]
- Four studies to date have evaluated the use of penicillin for penicillin-susceptible *Staphylococcus aureus* (PSSA)[3-6]

Purpose

- To evaluate the safety and efficacy of penicillin vs cefazolin or anti-staphylococcal penicillins in the treatment of PSSA bacteremia

Methods



Primary outcome	Secondary outcomes
Composite 60-day clinical failure: • Change in antimicrobials after at least 72 hours of definitive therapy • Recurrence of PSSA bacteremia • Infection-related readmission • All-cause mortality	• Hospital length of stay • Treatment duration • Duration of bacteremia • Adverse events • 30- and 90-day microbiologic recurrence and mortality

- Pearson chi-squared and Kaplan-Meier survival were used to compare the primary outcome between interventions

Results

Baseline Characteristics	Penicillin (n=49)	Cefazolin (n=26)	ASPs (n=26)
Age, median (IQR), years	60 (43-70.5)	59.5 (49.5-68.5)	59.5 (35.5-71)
Male	31 (63.2)	13 (50)	18 (69.2)
Hardware	19 (38.7)	9 (34.6)	12 (46.1)
Intravenous line	12 (24.4)	9 (34.6)	4 (15.3)
Dialysis	2 (4)	3 (11.5)	1 (3.8)
Persons who inject drugs	7 (14.2)	10 (38.5)	6 (23)
Pitt bacteremia score, median (IQR)	1 (0-4)	1 (0-4)	2 (0-3.25)
Charlson comorbidity score, median (IQR)	3 (2-6)	6 (3.75-7.25)	5 (3-9)
ICU admission within 72 hours of positive blood culture	11 (22.4)	9 (34.6)	6 (23)
Source of bacteremia:			
Skin & soft tissue infection	14 (28.5)	7 (26.9)	6 (26)
Central line	6 (12.2)	6 (23.1)	3 (11.5)
Injection drug use	1 (2)	0	0
Dentition	0	0	1 (3.8)
Unknown	28 (57.1)	13 (50)	16 (61.5)
Secondary infections:			
Endocarditis	6 (12.2)	1 (3.8)	5 (19.2)
Osteomyelitis	1 (2)	1 (3.8)	4 (15.3)
Other	7 (14.2)	0	1 (3.8)
None	35 (71.4)	24 (92.3)	16 (61.5)

*Data presented as n (%) unless otherwise indicated

Primary Outcome	Penicillin (n=49)	Cefazolin (n=26)	ASPs (n=26)
60-day clinical failure	14 (28.6)	5 (19.2) (p=0.376 vs penicillin)	14 (53.8) (p=0.031 vs penicillin)
Change in antimicrobial	11 (22.4)	4 (15.3)	11 (42.3)
Recurrence of bacteremia	2 (4)	0 (0)	1 (3.8)
Infection-related readmission	2 (4)	1 (3.8)	3 (11.5)
All-cause mortality	1 (2)	0 (0)	3 (11.5)

*Data presented as n (%)

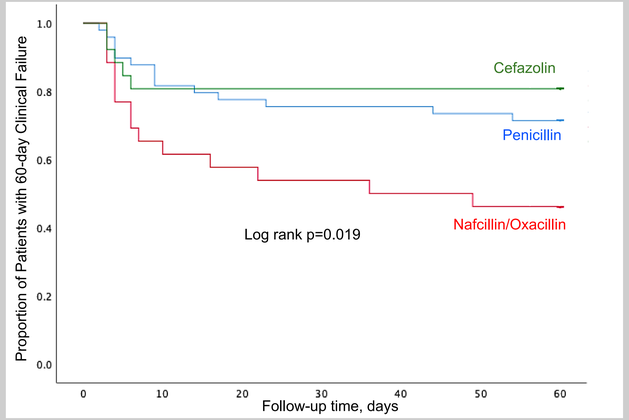


Figure. Kaplan-Meier estimate curve for patients treated with penicillin, cefazolin and nafcillin/oxacillin for the 60-day clinical failure composite outcome

Secondary Outcomes	Penicillin (n=49)	Cefazolin (n=26)	ASPs (n=26)
Length of stay, days, mean ± SD	15.4 ± 13.7	15.1 ± 13.9	16.1 ± 14.3
Duration of bacteremia, days, mean ± SD	7.9 ± 4.1	8.0 ± 4.4	8.0 ± 4.4
Treatment duration, days, mean ± SD	33.3 ± 15.6	31.9 ± 14.9	33.4 ± 15.2
30-day:			
Bacteremia recurrence	1 (2)	0	0
All-cause mortality	1 (2)	0	2 (7.6)
90-day:			
Bacteremia recurrence	2 (4)	0	1 (3.8)
All-cause mortality	1 (2)	0	3 (11.5)
Adverse Events	**Penicillin**	**Cefazolin**	**ASPs**
Acute interstitial nephritis	2 (4)	1 (3.8)	4 (15.3)
Rash	3 (6.1)	0	0
Hepatotoxicity	0	0	1 (3.8)
Hypernatremia	0	0	1 (3.8)
Other	4 (8.1)	1 (3.8)	0

*Data presented as n (%) unless otherwise indicated

Discussion

- The higher rate of 60-day clinical failure with ASPs in comparison to penicillin was driven primarily by changes in antibiotic regimen
- A non-significant higher mortality rate was observed among PSSA bacteremia patients who were treated with ASPs in comparison to penicillin, while cefazolin had a similar mortality rate to penicillin
- Discontinuation due to an adverse event was higher with nafcillin/oxacillin (23%) in comparison to penicillin (18.3%) and cefazolin (7.6%)
- Patients treated with anti-staphylococcal penicillins had numerically more secondary infections in comparison to patients treated with penicillin and cefazolin

Limitations

- Retrospective analysis which cannot control for potential treatment biases (confounding by indication)
- Nafcillin and oxacillin groups were combined as only three patients were treated with oxacillin
- Results can only be generalized to institutions that perform penicillin susceptibility testing

Conclusion

- Penicillin is safe and effective for the treatment of PSSA bacteremia in comparison to cefazolin and may be preferable to anti-staphylococcal penicillins

Disclosure

The authors have nothing to disclose

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