Poster # 1071

Treatment Outcomes with Nafcillin versus Cefazolin for Methicillin-Susceptible *Staphylococcus aureus* Bloodstream Infections

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Abstract

Background: Historically, nafcillin (NAF) and oxacillin have been drugs of choice for the treatment of methicillin-susceptible *Staphylococcus aureus* (MSSA) infections. Cefazolin (CFZ) is an alternative in patients unable to tolerate antistaphylococcal penicillins, and data from small retrospective studies suggest that CFZ may have similar efficacy in the treatment of MSSA bloodstream infections (BSI). We compared rates of treatment failure and adverse effects associated with the use of NAF and CFZ for MSSA BSI at a large academic medical center.

Methods: Adult inpatients with ≥ 1 blood culture positive for MSSA between 7/1/2011 and 8/31/2015 were candidates for inclusion in this retrospective cohort study. Patients were included if they received ≥ 72 hours of NAF or CFZ as directed therapy after receiving ≤ 72 hours of any empiric therapy. Patients were excluded if they received antibiotics active against MSSA other than NAF or CFZ, had a polymicrobial index BSI, or had a BSI due to any pathogen within the previous 30 days. The primary outcome was treatment failure, defined as clinician documentation of treatment failure for any reason, recurrence of MSSA infection within 30 days, or 30-day, all-cause, in-hospital mortality. Secondary outcomes included antibiotic-related acute kidney injury (AKI), acute interstitial nephritis (AIN), hepatotoxicity, and rash.

Results: Of 100 patients with MSSA BSI, 73 (73%) received NAF and 27 (27%) received CFZ. Baseline characteristics were similar among groups except CFZ patients had higher APACHE II scores (median 17 vs. 10; p < 0.01), a higher frequency of renal dysfunction (40.7% vs. 6.8%; p < 0.01), and a higher frequency of hemodialysis dependence (33.3% vs. 1.4%; p < 0.01). No differences in treatment failure (2.7% vs. 3.7%; p = 1.00) or clinical cure (76.7% vs. 70.4%; p = 0.60) rates were detected between the NAF and CFZ groups, respectively. Acute kidney injury was numerically more frequent in NAF patients (24.7% vs. 7.4%; p = 0.09).

Conclusions: No difference in treatment failure was observed between patients who received NAF or CFZ for MSSA BSI among this cohort. In light of the higher incidence of AKI among NAF patients, future studies evaluating CFZ as a preferred agent are warranted.

Background

- Nafcillin (NAF) and oxacillin (OXA) are drugs of choice for the treatment of MSSA BSI and have demonstrated superior efficacy over vancomycin
- Cefazolin (CFZ) is an acceptable alternative in patients unable to tolerate antistaphylococcal penicillins
- NAF and OXA have a narrower spectrum of activity compared to CFZ, however CFZ has a more convenient dosing regimen, has less reports of nephrotoxicity, and is less expensive than NAF and OXA

Objective

To compare rates of treatment failure associated with the use of NAF vs. CFZ for MSSA BSI among adult inpatients at Beth Israel Deaconess Medical Center (BIDMC)

Methods

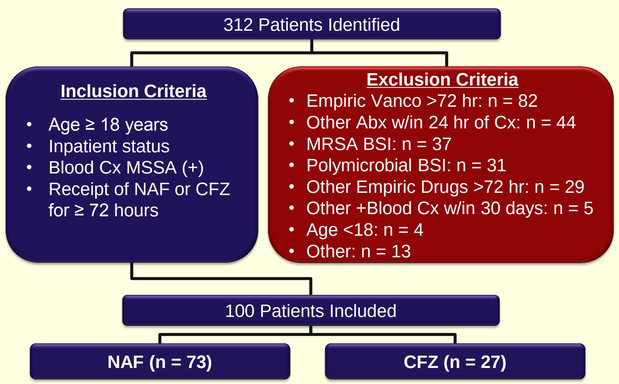
Design: Retrospective cohort study of adult inpatients with MSSA BSI who received ≥ 72 hours of treatment with NAF or CFZ

- This study was approved by the BIDMC institutional review board

Definitions:

Outcome	Definition
Treatment Failure **(Primary Outcome)**	One or more of the following: • Change in antibiotic therapy due to clinician's documentation that treatment had failed • Recurrence of MSSA infection within 30 days of treatment completion • All-cause, in-hospital mortality within 30 days of treatment completion
Acute Kidney Injury	An increase in serum creatinine (SCr) ≥ 0.5 mg/dL or a 50% increase from baseline during the hospital stay
Acute Interstitial Nephritis	Acute kidney injury and one or more of the following symptoms: • Leukocyturia • Hematuria • Proteinuria • Eosinophiluria (>1%) • Eosinophilia (>5%) • Fever (≥101°F or ≥100.4°F x >1 hr)
Hepatotoxicity	An increase in alanine aminotransferase (ALT) > 3 times the upper limit of normal
Rash	Clinician's documentation of rash that developed after initiation of antibiotic therapy

Results



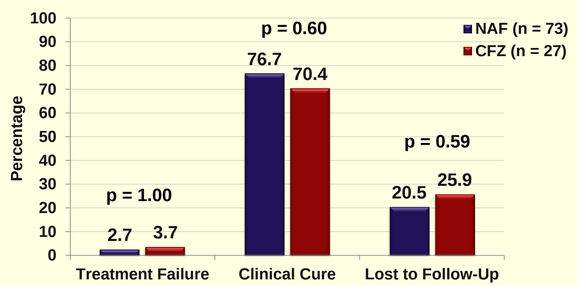
Results cont.

Patient Characteristics	NAF (n = 73)	CFZ (n = 27)	p-value
Age, mean ± SD	58 ± 15.2	56 ± 17.0	0.69
Male, n (%)	47 (64.4)	17 (63.0)	1.00
Length of Stay (days), median (IQR)	9 (7-12)	9 (6-16)	0.51
ICU Admission, n (%)	**17 (23.3)**	**12 (44.4)**	**<0.05**
APACHE II Score, median (IQR)	**10 (6-14)**	**17 (9-23)**	**<0.01**
Duration of BSI (days), median (IQR)	2 (1-3)	2 (1-2)	0.11
CrCl on Admission (mL/min), median (IQR)	84.3 (54.7-118.3)	46.8 (14.4-111.3)	0.08
Renal Dysfunction, n (%)	**5 (6.8)**	**11 (40.7)**	**<0.01**
HD Prior to Admission, n (%)	**1 (1.4)**	**9 (33.3)**	**<0.01**
Obesity (BMI ≥30), n (%)	31 (42.5)	10 (37.0)	0.65
Diabetes Mellitus, n (%)	15 (20.5)	10 (37.0)	0.12
IVDU, n (%)	8 (11.0)	4 (14.8)	0.73
Chemotherapy, n (%)	7 (9.6)	2 (7.4)	1.00
Hepatic Dysfunction, n (%)	6 (8.2)	3 (11.1)	0.70
Immunosuppression, n (%)	4 (5.5)	4 (14.8)	0.21

Source of BSI, n (%)	NAF (n = 73)*	CFZ (n = 27)*	p-value
Bone & Joint	26 (35.6)	7 (25.9)	0.47
Endocarditis	12 (16.4)	3 (11.1)	0.75
Central-Line Associated BSI	9 (12.3)	5 (18.5)	0.52
Skin and Soft Tissue	8 (11.0)	3 (11.1)	1.00
Surgical Site	3 (4.1)	0 (0)	0.56
Pneumonia	2 (2.7)	1 (3.7)	1.00
Other	11 (15.1)	2 (7.4)	0.50
Undetermined	7 (9.6)	7 (25.9)	0.05

* 5 NAF patients had 2 sources each, 1 CFZ patient had 2 sources

Primary Outcome:



Results cont.

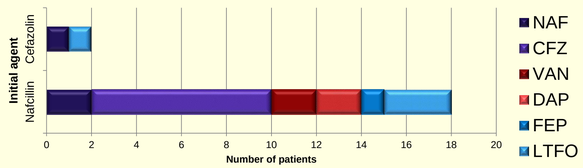
Secondary Outcomes:

Outcome, n (%)	NAF (n = 73)	CFZ (n = 27)	p-value
Acute Kidney Injury	18 (24.7)	2 (7.4)	0.09
Acute Interstitial Nephritis	8 (11.0)	0 (0)	0.10
Rash	6 (8.2)	1 (3.7)	0.67
Hepatotoxicity	3 (4.1)	0 (0)	0.56

Subanalysis of Patients with Acute Kidney Injury:

	NAF (n = 18)	CFZ (n = 2)
Change in Scr (mg/dL), median (IQR)	1.0 (0.6-1.8)	0.6 (0.5-0.6)
Treatment Failure, n (%)	1 (5.6)	0 (0)
Clinical Cure, n (%)	15 (83.3)	2 (100)
Lost to Follow-Up, n (%)	2 (11.1)	0 (0)

Definitive Therapy Following Acute Kidney Injury:



Van: vancomycin; DAP: daptomycin; FEP: cefepime; LTFO: lost to follow up

Conclusions

- Patients receiving CFZ were more likely to have higher APACHE II scores, be admitted to an ICU, and have underlying renal impairment
- No significant differences in treatment failure rates were seen in patients receiving NAF vs. CFZ for MSSA BSI in this study.
- Incidences of AKI, AIN, rash, and hepatotoxicity were numerically more frequent in the NAF group.
- In patients developing AKI on NAF, many were able to tolerate a switch to CFZ
- Larger prospective studies evaluating CFZ as a preferred agent for the treatment of MSSA BSI are warranted.

Disclosures

The authors of the presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

CC Burrelli, HS Gold, GM Snyder: Nothing to disclose
EB Hirsch, C McCoy, MV Mahoney: Actavis (Investigator) and Theravance (Consultant)
EB Hirsch: The Medicines Company (Scientific Advisor)