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Abstract (modified)

Background: *Staphylococcus aureus* blood stream infections (BSIs) are associated with significant mortality and healthcare costs. Methicillin sensitive *S. aureus* (MSSA) BSIs may be treated with cefazolin or an anti-staphylococcal penicillin as first-line options (standard therapy [ST]); however, other agents with reported susceptibility may also be considered for use based on convenience of dosing, concomitant infecting organisms, or patient allergies. The purpose of this study was to evaluate the comparative efficacy of ST versus other beta-lactam therapy (OBT) in treating MSSA BSIs.

Methods: This was a retrospective, cohort study of patients with MSSA BSIs treated with beta-lactam antibiotics as definitive therapy at an academic medical center between January 2012 and December 2014. Patients ≥ 18 years of age at time of culture treated with definitive beta-lactam therapy for at least 48 hours were included in two groups: ST or OBT. The primary outcome was time to microbiological cure, measured as time to negative blood cultures. Secondary outcomes included infection recurrence, hospital length of stay, intensive care unit (ICU) length of stay, and inpatient mortality.

Results: 192 patients were included in this study: 152 in the ST group and 40 in the OBT group. Baseline demographic data was similar between groups. The primary outcome of time to negative blood cultures was not statistically significantly different between groups (2 days vs 2.5 days; p=0.72). Patients in the ST group had numerically shorter median ICU length of stay than patients in the OBT group (3 days vs. 7 days, p=0.11). There was significantly lower all-cause in-house mortality in the ST group with 4 deaths compared to 9 deaths in the other OBT group (p<0.01). There was no statistically significant difference between groups with regard to infection recurrence and length of hospital stay (p=0.58, p=0.08, respectively).

Conclusion: For patients with MSSA BSIs, ST and OBT showed similar time to negative blood cultures. ST was associated with reduced in-house mortality. Future studies are needed to determine the contribution of specific non-ST beta-lactam agents to the outcomes of interest.

Introduction

- Historically, oxacillin and nafcillin have been considered standard treatment for MSSA blood stream infections (BSIs)
- Cefazolin has been shown to have comparable clinical efficacy to oxacillin and nafcillin in treating MSSA BSI
- Studies conducted due to unavailability of oxacillin and nafcillin
 - Cefazolin discontinued less frequently than nafcillin
- Penicillin binding protein binding affinity of various beta-lactams may contribute to the varying efficacy against MSSA
- Existing literature is conflicting and there have been no randomized controlled trials comparing different beta-lactams for treatment of MSSA infections

Objective

- To evaluate the comparative efficacy of standard therapy (cefazolin or anti-staphylococcal penicillin) versus other beta-lactam therapy (OBT) in treating MSSA BSIs

Methods

Study Design

- Retrospective, cohort study

Patient Selection

- Inclusion Criteria
 - > 18 years of age
 - Positive MSSA blood culture between January 2012 to December 2014
 - Beta-lactam as definitive treatment (for at least 48 hours)
- Exclusion Criteria
 - Polymicrobial bloodstream infection
 - Pregnancy

Outcomes

- Primary: Time to negative blood cultures
- Secondary: Infection recurrence, hospital length of stay, ICU length of stay, inpatient mortality

Statistical Analysis

- Chi-square, Fisher's exact, Student's T-test, and Wilcoxon Rank-sum were used in analyses as appropriate
- All statistical analyses were performed with Intercooled Stata, version 13 (Statacorp, College Station, TX)

Results (continued)

Table 1. Patient Demographics

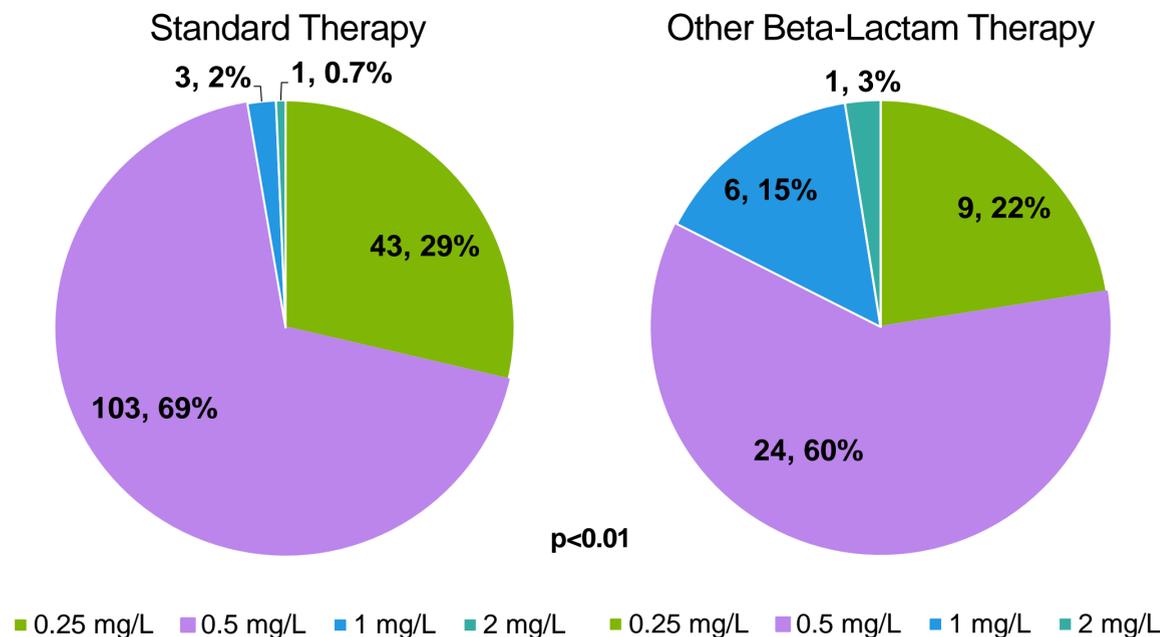
	Other Treatment n=40	Standard of Care Treatment n=152	p-value
Age (mean,SD)	58.9 (2.2)	59.4 (1.3)	0.86
Gender, female (n,%)	14 (35)	61 (40.4)	0.53
Race (n,%)			
Caucasian	27 (67.5)	79 (52)	0.08
Hispanic	1 (2.5)	8 (5.3)	0.69
African American	9 (22.5)	38 (25)	0.74
Asian	0 (0)	4 (2.6)	0.58
Other	3 (7.5)	23 (15.1)	0.30
Weight, kg (median,IQR)	81.6 (69.6-94)	79.4 (63.8-95.1)	0.55
ANC (median, IQR)	6.2 (3.4-12.3)	8.4 (5.1-12.5)	0.21
Neutropenic (n,%)	3 (8.6)	11 (8)	0.99
APACHE II (median, IQR)	15.5 (10-22)	14 (9-19)	0.39
CrCl ≥ 60 mL/min (n,%)	25 (62.5)	80 (52.6)	0.27
ICU transfer (n,%)	22 (55)	62 (40.8)	0.11
ID Consult (n,%)	31 (77.5)	131 (86.2)	0.18

Table 2. Patient Outcomes

	Other Treatment n=40	Standard of Care Treatment n=152	p-value
Time to negative blood cultures, days (median, IQR)	2.5 (2-3)	2 (2-3)	0.72
Negative blood cultures (n,%)	40 (100)	151 (99.3)	0.99
BSI Source (n,%)			
Line associated	6 (15)	32 (21)	0.50
Hardware associated	3 (7.5)	22 (14.5)	0.30
Other	24 (60)	69 (45.4)	0.10
MSSA at other site (n,%)	23 (57.5)	85 (55.9)	0.86
Other Site Source (n,%)			0.20
Lung	5 (12.5)	9 (5.9)	
Urine	7 (17.5)	18 (11.8)	
Wound	4 (10)	31 (20.4)	
Cath Tip	2 (5)	18 (11.8)	
Fluid	5 (12.5)	11 (7.2)	
Infection recurrence (n,%)	0 (0)	4 (2.8)	0.58
Length of hospital stay, days (median, IQR)	16 (7.5-29.5)	11 (7.5-18.5)	0.08
Length of ICU stay, days (median, IQR)	7 (3-19)	3 (2-8)	0.11
Inpatient mortality (n,%)	9 (22.5)	4 (2.6)	<0.01

Results

Figure 1. Oxacillin Minimum Inhibitory Concentrations



Conclusions

- No difference found in time to negative cultures between ST and OBT
- ST was associated with a reduced inpatient mortality
- Further studies are required to establish the contribution of specific non-ST beta-lactam agents to the outcomes of interest