Comparison of clinical outcomes for glycopeptides and beta-lactams in methicillin-susceptible *Staphylococcus aureus* bloodstream infections

Yeon Ju La[1], Hye Rim Kim[2], Dong Hyun Oh[3], Jin Young Ahn[4]* and Yong Chan Kim[4]*

[1]Department of Internal Medicine, Kangwon National University Hospital, Gangwon-do, Republic of Korea
[2]Biostatistics Collaboration Unit, Department of Biomedical Systems Informatics, Yonsei University College of Medicine, Seoul, Republic of Korea
[3]Department of Internal Medicine, Seoul Medical Center, Seoul, Republic of Korea
[4]Division of Infectious Diseases, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea

Background

Several studies demonstrated the inferiority of glycopeptides as definitive antibiotics for MSSA BSI compared to anti-staphylococcal beta-lactam antibiotics. However, almost all of them were retrospective observational studies and no randomized controlled. Therefore, there remains the problem of bias in treatment selection and the possibility of residual confounding factors. In this study, we compare the therapeutic effects of glycopeptides and anti-staphylococcal beta-lactams in the treatment of MSSA BSI using inverse probability of treatment weighting (IPTW) analysis.

Methods

This is a retrospective cohort study performed in double-center from January 1, 2010 to December 31, 2018. Patients (age ≥18 years) with MSSA identified in the blood culture were included. Patients were classified into two groups according to definite antibiotics used, the beta-lactam (nafcillin or cefazolin) group and the glycopeptide (vancomycin or teicoplanin) group.

Results

During the study period, 643 patients had MSSA bacteremia. Among them, 203 were treated with beta-lactam group and 156 were treated with glycopeptide group as definite therapy. (Figure 1). Comparison of clinical characteristics of patients between the beta-lactam and glycopeptide groups are shown in Table 1. After IPTW, baseline characteristics of the two groups were well balanced except for the primary focus of bacteremia. Although persistent bacteremia was less common in glycopeptide group (17.9% vs 4.0%; OR, 0.28; 95% CI, 0.14 – 0.60; P < 0.001), the glycopeptide group had higher overall mortality rate (15.9% vs 39.6%, P = 0.024), 7-day mortality rate (2.1% vs 14.1%, P < 0.001), and 28-day mortality rate (7.7% vs 30.9%, P = 0.012) (Table 2) than those of the beta-lactam group. When IPTW was augmented by multivariable logistic regression analyses to minimize remnant confounding, glycopeptide use for the treatment of MSSA BSI was associated with significant risk for 28-day mortality (adjusted OR, 3.37; 95% CI, 1.71–6.61; P < 0.001) (Figure 2).

Conclusions

Definitive therapy with beta-lactams in patients with MSSA BSI was associated with lower 28-day mortality when compared with definitive therapy with glycopeptides. This study provides compelling evidence of anti-staphylococcal beta-lactam use for MSSA BSI treatment.

Tables and figures

Figure 1. Flow chart of the study population

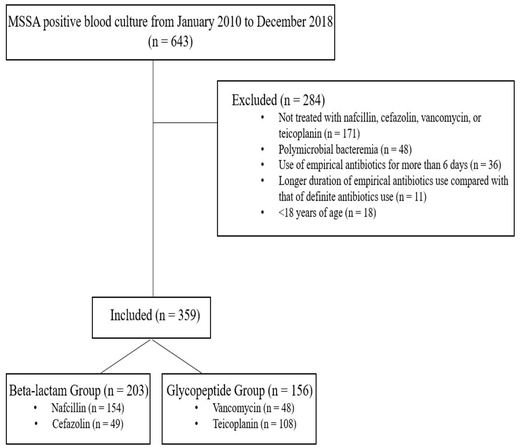
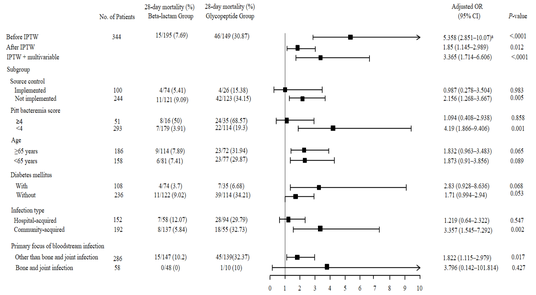


Figure 2. Adjusted ORs and 95% CIs for the primary end point in main analysis and various subgroups



Abbreviations: CI, confidence interval; OR, odds ratio; IPTW, inverse probability of treatment weighting.
aUnadjusted OR

Table 1. Baseline characteristics of patients who received anti-staphylococcal beta-lactams or glycopeptides as definitive therapy

Variables	Beta-lactam Group[a] (*n* = 203)	Glycopeptide Group[a] (*n* = 156)	*P*-value
Demographic			
Female, no. (%)	69 (34)	64 (41)	0.171
Age, years	65.4 ± 14.5	62.6 ± 16.9	0.090
Body mass index, kg/m^2	22.9 ± 4.4	22 ± 4	0.069
Laboratory			
White blood cell count per mm^3	12890.8 ± 7241.2	12442.3 ± 10098.7	0.639
Platelet per mm^3	209379.3 ± 127822.9	191897.4 ± 131145.5	0.205
Creatinine, mg/dL	1.6 ± 1.8	1.6 ± 2.1	0.768
Total bilirubin, mg/dL	1.2 ± 1.4	1.5 ± 2.9	0.241
Albumin, g/dL	3.1 ± 0.7	3 ± 0.8	0.562
C-reactive protein, mg/L	157.8 ± 105.8	120.2 ± 95.8	0.001
Comorbidity			
Congestive heart failure, no. (%)	22 (10.8)	24 (15.4)	0.201
Peripheral vascular disease, no. (%)	9 (4.4)	4 (2.6)	0.347
Coronary artery obstructive disease, no. (%)	26 (12.8)	18 (11.5)	0.716
Cerebrovascular accident, no. (%)	24 (11.8)	12 (7.7)	0.197
Dementia, no. (%)	3 (1.5)	4 (2.6)	0.474*
Hemiplegia, no. (%)	6 (3)	4 (2.6)	>.999*
Pulmonary disease, no. (%)	21 (10.3)	16 (10.3)	0.978
Connective tissue disease, no. (%)	5 (2.5)	5 (3.2)	0.752*
Liver disease, no. (%)	25 (12.3)	25 (16)	0.314
Diabetes mellitus, no. (%)	74 (36.5)	37 (23.7)	0.01
Renal disease, no. (%)	41 (20.2)	26 (16.7)	0.395
Hemodialysis, no. (%)	17 (8.4)	7 (4.5)	0.144
Cancer, no. (%)	50 (24.6)	83 (53.2)	<.0001
Hospital acquired infection, no. (%)	60 (29.6)	98 (62.8)	<.0001
Pitt bacteremia score	1.2 ± 2.6	2.7 ± 4	<.0001
Source control, yes (%)	79 (38.9)	26 (16.7)	<.0001
Metastatic infection, yes (%)	32 (15.8)	15 (9.6)	0.087
Primary focus of bloodstream infection			<.0001
Catheter-related, no. (%)	21 (10.3)	12 (7.7)	
Pneumonia, no. (%)	10 (4.9)	17 (10.9)	
Urinary tract, no. (%)	15 (7.4)	5 (3.2)	
Skin and soft tissue, no. (%)	62 (30.5)	22 (14.1)	
Bone and joint, no. (%)	49 (24.1)	10 (6.4)	
Intra-abdominal, no. (%)	6 (3)	20 (12.8)	
Others[b], no. (%)	40 (19.7)	70 (44.9)	

[a]Variables are displayed as mean ± standard deviation unless otherwise specified.
[b]Others include central nervous system infections, gastroenteritis, deep neck infection, and focus unknown.
*Fisher's exact test

Table 2. Comparison of clinical outcomes between beta-lactam group and glycopeptide group after inverse probability of treatment weighting

Variables	Beta-lactam Group (*n* = 195[†])	Glycopeptide Group (*n* = 149[†])	Odds Ratio* (95% CI)	*P*-value
Recurrent bloodstream infection, no. (%)	5 (2.6)	6 (4.0)	1.253 (0.325 – 4.828)	0.743
Recurrence within 30 days	1 (0.5)	3 (2.0)	2.855 (0.23 – 35.459)	0.414
Recurrence within 90 days (31 days to 90 days)	4 (2.1)	3 (2.0)	0.836 (0.156 – 4.482)	0.835
Persistent bloodstream infection, no. (%)	35 (17.9)	6 (4.0)	0.283 (0.135 – 0.595)	0.001
ICU admission after infection, no. (%)	38 (19.5)	31 (20.8)	1.35 (0.838 – 2.174)	0.217
Mortality, no. (%)	31 (15.9)	59 (39.6)	1.64 (1.068 – 2.519)	0.024
Death within 7 days	4 (2.1)	21 (14.1)	5.174 (2.083 – 12.85)	<0.001
Death within 28 days (8 days to 28 days)	15 (7.7)	46 (30.9)	1.85 (1.145 – 2.989)	0.012
Drug adverse event, no. (%)	28 (14.4)	9 (6.0)	0.471 (0.244 – 0.91)	0.025

CI, confidence interval; ICU, intensive care unit.
†A total of 15 cases with insufficient data for adjustment (inverse probability of treatment weighting) were excluded.
*The odds ratio for glycopeptide group compared with beta-lactam group was calculated by weighted logistic regression model using inverse probability of treatment weighting.