Non-Carbapenem Antimicrobials for ESBL-Producing Enterobacteriaceae Bacteremia: A Single-Center Retrospective Study

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Background

• Extended-spectrum β-lactamase–producing Enterobacteriaceae (ESBL-E) bacteremia is increasingly common and creates a substantial clinical and economic burden

• Carbapenems are the standard of care for ESBL-E bacteremia, but their widespread use accelerates the emergence of carbapenem-resistant Enterobacteriaceae

• In vitro and retrospective data suggest that selected non-carbapenem agents, especially piperacillin-tazobactam (PIP/TAZ), may remain useful in susceptible ESBL-E infections

• In South Korea, the need for carbapenem-sparing strategies is clinically important because ESBL-E prevalence has remained high and antimicrobial stewardship is increasingly relevant

• This study evaluated whether non-carbapenem antimicrobials were associated with different clinical outcomes from carbapenems in adults with ESBL-E bacteremia

Methods

• Single-center retrospective case-control study using electronic medical records from Jeju National University Hospital, South Korea

• Study period: January 1 to December 30, 2021. Adults (≥18 years) with documented ESBL-E bacteremia were reviewed

• After exclusions, 118 patients were analyzed: 54 in the non-carbapenem group (NCG) and 64 in the carbapenem group (CG)

• Definitive therapy determined group allocation. Non-carbapenem therapy included PIP/TAZ and other non-carbapenem agents

• Primary outcome: treatment failure at 30 days. Secondary outcome: 30-day all-cause mortality

• Additional outcomes included microbiologic failure, duration of hospitalization, and duration of antimicrobial therapy

• Kaplan-Meier analysis and Cox regression were used for outcome comparison. Multivariate logistic regression identified independent risk factors for treatment failure

Key Results

• 118 patients with ESBL-E bacteremia were included (NCG 54; CG 64). The most common pathogen was Escherichia coli, and urinary tract infection was the predominant source in both groups

• Treatment failure at 30 days: 16.7% in NCG vs. 18.8% in CG (p=0.65).

• 30-day all-cause mortality: 14.8% in NCG vs. 17.2% in CG (p=0.63)

• Cox regression showed no significant between-group difference in treatment failure (HR 1.32, 95% CI 0.55–3.17) or mortality (HR 1.75, 95% CI 0.51–6.05)

• Length of hospital stay was significantly shorter in NCG (11.5 [7.0–16.0] days) than in CG (16.0 [11.5–28.0] days; p=0.009)

Conclusion

• Treatment failure at 30 days and 30-day mortality did not differ significantly between non-carbapenem and carbapenem therapy groups

• Hospitalization duration was shorter in the non-carbapenem group

• Extra-urinary tract infection and prior antimicrobial therapy within 30 days were independent risk factors for treatment failure

• These findings support selective use of non-carbapenem antimicrobials, including PIP/TAZ, in mild-to-moderate ESBL-E bacteremia while helping reduce carbapenem pressure

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Table 1. Clinical characteristics of patients with ESBL-E bacteremia

Variable	Carbapenem group (n=64)	Non-carbapenem group (n=54)	p-value
Male	35 (54.7)	19 (35.2)	0.042
Age, years	75.0 ± 12.5	79.4 ± 12.3	0.058
DM	24 (37.5)	21 (38.9)	1.000
CKD	11 (17.2)	6 (11.1)	0.501
Malignancy	18 (28.1)	11 (20.4)	0.447
Pitt score	1.0 (0.0–2.0)	1.0 (0.0–2.0)	0.599
Hospital-acquired infection	16 (21.9)	14 (25.9)	0.787
ICU admission	22 (34.4)	15 (27.8)	0.568
Urinary tract source	34 (53.1)	35 (64.8)	
Biliary tract source	11 (17.2)	9 (16.7)	
Escherichia coli	44 (68.8)	40 (74.1)	
Klebsiella pneumoniae	17 (26.6)	8 (14.8)	
PIP/TAZ definitive therapy	0 (0.0)	25 (46.3)	
Duration of antibiotics	14.0 (10.0–16.0)	13.0 (10.7–15.2)	0.975
Length of hospital stay	16.0 (11.5–28.0)	11.5 (7.0–16.0)	0.009
Primary outcome	12 (18.8)	9 (16.7)	0.958
Secondary outcome	11 (17.2)	8 (14.8)	0.592

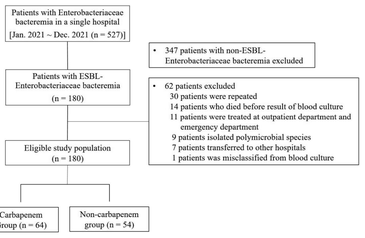
Values are number (%), mean ± SD, or median (IQR). DM, diabetes mellitus; CKD, chronic kidney disease; ICU, intensive care unit.

Table 2. Risk factors for treatment failure

Variable	Univariate OR (95% CI)	p	Multivariate OR (95% CI)	p
≥80 years old	1.841 (0.691–4.901)	0.190	1.023 (0.310–3.370)	0.971
Female	2.582 (0.947–7.037)	0.060	0.494 (0.151–1.619)	0.244
Diabetes	0.490 (0.099–2.400)	0.386		
Chronic kidney disease	1.627 (0.341–7.748)	0.541		
Malignant cancer	4.158 (1.515–11.410)	0.060	2.263 (0.639–8.014)	0.206
Prior hospitalization ≤30 days	2.266 (0.843–6.089)	0.105	0.429 (0.092–2.012)	0.283
Prior antimicrobial therapy ≤30 days	4.891 (1.783–13.419)	0.002	5.153 (1.255–21.158)	0.023
Hospital-acquired infection	4.500 (0.867–23.345)	0.073	1.021 (0.090–11.594)	0.987
ICU admission	1.586 (0.587–4.287)	0.363		
Pitt bacteremia score ≥5	2.526 (0.218–29.217)	0.459		
Non-carbapenem group	0.964 (0.367–2.533)	0.940	1.897 (0.586–6.142)	0.286
Extra-urinary tract infection	4.391 (1.548–12.462)	0.005	3.247 (1.001–10.531)	0.049
PIP/TAZ MIC ≥32 μg/mL	2.668 (0.984–7.232)	0.054	1.295 (0.359–4.668)	0.692
Klebsiella pneumoniae	3.176 (1.127–8.953)	0.029	1.954 (0.558–6.842)	0.295

Independent risk factors were extra-urinary tract infection and prior antimicrobial therapy within 30 days.

Figure 1. Study population



Flow diagram of patient selection: 527 Enterobacteriaceae bacteremia cases screened; 118 ESBL-E bacteremia patients included.

Figure 2. Kaplan-Meier analysis

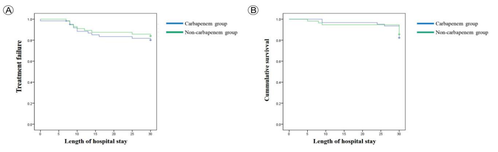


Figure 2. Survival of patients with extended-spectrum β-lactamase (ESBL)-*Enterobacteriaceae* bacteremia in the carbapenem and non-carbapenem groups by Kaplan-Meier analysis. (A) Treatment failure at 30 days, (B) 30-day mortality rate.

No significant between-group difference in 30-day treatment failure or 30-day mortality.

Figure 3. Cox regression analysis

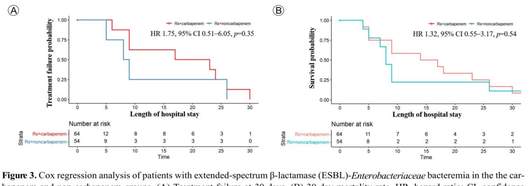


Figure 3. Cox regression analysis of patients with extended-spectrum β-lactamase (ESBL)-*Enterobacteriaceae* bacteremia in the the carbapenem and non-carbapenem groups. (A) Treatment failure at 30 days, (B) 30-day mortality rate. HR, hazard ratio; CI, confidence interval.

Cox regression showed no significant difference in treatment failure or mortality between carbapenem and non-carbapenem groups.

Clinical Implications and Limitations

• Clinical outcomes were comparable between carbapenem and non-carbapenem therapy groups despite the prevailing preference for carbapenems in ESBL-E bacteremia

• The shorter hospital stay in the non-carbapenem group suggests a potential practical advantage in appropriately selected patients

• Higher-risk features for treatment failure were extra-urinary tract infection and prior antimicrobial therapy within 30 days; these patients may require closer monitoring and optimized source control

• The study population was predominantly mild-to-moderate disease severity, and the effectiveness of non-carbapenem therapy in severe disease remains uncertain

• This was a single-center retrospective study with a limited sample size; further large prospective multicenter studies are required to refine treatment strategies

Selective use of non-carbapenem therapy may help preserve carbapenem efficacy in mild-to-moderate ESBL-E bacteremia.