Cefepime versus carbapenems for the treatment of ESBL-producing *Enterobacterales* among non-blood isolates

Brandon Garcia, PharmD[1,3]; Alexandra Hanretty, PharmD[2,3]; Geena Kludjian, PharmD[3]; Madeline King, PharmD[1,2,3]
[1]Philadelphia College of Pharmacy, Philadelphia, PA; [2]Cooper Medical School of Rowan University, Camden, NJ; [3]Cooper University Hospital, Camden, NJ

Background

- The incidence of organisms harboring extended-spectrum beta-lactamases (ESBLs) have been increasing
- Excess carbapenem use has been associated with selection for carbapenem-resistant *Enterobacterales*
- The data available for the use of cefepime in ESBL-producing *Enterobacterales* is limited to small observational studies with mixed results
  - May be attributed to factors such as:
    - Elevated minimum inhibitory concentration (MIC) values based on outdated breakpoints
    - Suboptimal dosing regimens
    - Source of infection

The aim of this study is to compare the efficacy of cefepime versus carbapenems for the treatment of ESBL-producing *Enterobacterales* with an MIC ≤2 mcg/mL for non-bloodstream infections

Methods

- **Design:** Retrospective, single-center, cohort study from 1/1/2011 – 9/30/2021

Inclusion Criteria
- ≥ 18 years old
- Cefepime or carbapenem for ≥ 72 hours
- ESBL screen (+) or ceftriaxone resistance
- MIC ≤ 2 mcg/mL to cefepime or susceptible to carbapenem

Exclusion Criteria
- Bacteremia
- Polymicrobial infection non-susceptible to both arms
- Expiration within 48 hours of initial culture collection
- Nonremovable focus of infection
- Additional active agent

- **Primary endpoint:**
  - Clinical failure defined as persistence of symptoms requiring escalation of therapy or death
- **Secondary endpoints:** 14-day infection-related mortality, 30-day recurrence

Results

Table 1. Results

	Cefepime (n = 22)	Carbapenem (n = 78)	OR (*P* value; 95% CI)
Age*	67 (57 – 84.5)	64.5 (50.3 – 75)	
Male¥	7 (31.8)	31 (39.7)	
Updated Charlson Comorbidity Index*	2 (1 - 3)	2.5 (1 – 4)	
Source¥			
Urinary	18 (81.8)	76 (97.4)	
Intrabdominal	0 (0)	5 (6.4)	
Pulmonary	5 (22.7)	0 (0)	
Bone	0 (0)	1 (1.3)	
ESBL-confirmatory test positive¥	15 (68.2)	74 (94.9)	
ICU stay¥	9 (40.9)	12 (15.4)	
Definitive treatment length, days*	6 (5 – 7)	6.5 (5 – 10)	
Length of stay, days*	12.5 (7.3 - 19)	8 (6 – 12)	
Clinical failure¥	3 (13.6)	5 (6.4)	2.31 (0.28; 0.51 – 10.52)
14-day infection-related mortality¥	1 (4.5)	0 (0)	N/A
30-day recurrence¥	3 (13.6)	12 (15.4)	0.87 (0.84; 0.22 – 3.4)

*median (IQR)
¥n (%)

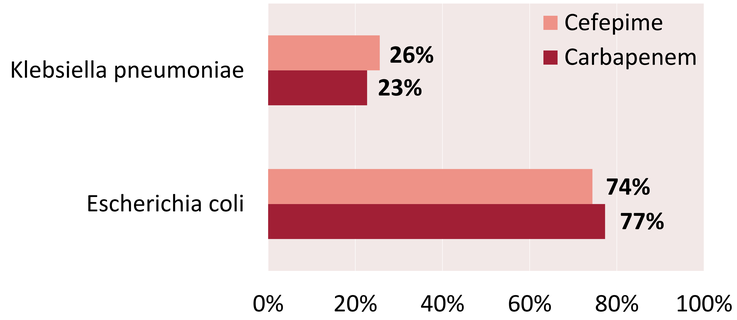
Table 2. Results with Cefepime MIC ≤2 mcg/mL

	Cefepime (n = 22)	Carbapenem (n = 20)	OR (*P* value; 95% CI)
Age, years*	67 (57 – 84.5)	70.5 (53.8 – 79.3)	
Updated Charlson Comorbidity Index*	2 (1 - 3)	2 (1 – 5.3)	
Source¥			
Urinary	18 (81.8)	19 (95)	
Intrabdominal	0 (0)	2 (10)	
Pulmonary	5 (22.7)	0 (0)	
ESBL-confirmatory test positive	15 (68.2)	18 (90)	
ICU stay¥	9 (40.9)	2 (10)	
Definitive treatment length, days*	6 (5 – 7)	5 (3 – 7)	
Length of stay, days*	12.5 (7.3 - 19)	6.5 (4.8 – 9)	
Clinical failure¥	3 (13.6)	0 (0)	N/A
14-day infection-related mortality¥	1 (4.5)	0 (0)	N/A
30-day recurrence¥	3 (13.6)	4 (20)	0.63 (0.58; 0.12 – 3.24)

*median (IQR)
¥n (%)

Results

Figure 1. Microbiology (n = 102)



Conclusion

Cefepime displayed numerically higher rates of clinical failure
- Larger portion of ICU patients in cefepime arm
- Recurrence rates numerically lower with cefepime
- Two of three cefepime failures were pulmonary infections

Large, prospective trials are needed to confirm findings
- Larger sample sizes to confirm or deny findings
- Larger data set for non-urinary sources
- Prospective randomization

Limitations

- Single-center, retrospective study
- Lack of follow-up information for discharged patients
- Small sample size
- Cannot discriminate between colonization and infection
- Confounding by indication

References

- Patel HB, Lusk KA, Cota JM. The role of cefepime in the treatment of extended-spectrum beta-lactamase infections. J Pharm Pract. 2019;32(4):458-463.
- Tamma PD, Rodriguez-Bano J. The use of noncarbapenem β-lactams for the treatment of extended-spectrum β-lactamase infections. Clin Infect Dis. 2017;64(7):972-80.
- Anderson DT, Albrecht B, Jones KA, et al. Efficacy of noncarbapenem B-lactams compared to carbapenems for extended-spectrum B-lactamase-producing Enterobacterales urinary tract infections. Open Forum Infect Dis. 2022;9(3):ofac034.