Third-Generation Cephalosporins Versus Carbapenems for Empiric Treatment of *Enterobacter* spp., *Serratia* spp., *Citrobacter* spp., or *Morganella morganii* Infections

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Key Lesson: No difference in early clinical failure between third-generation cephalosporins versus carbapenems

Purpose of Study

- Controversy exists on whether the use of third-generation cephalosporins to treat infections caused by *ampC*-inducible organisms lead to increased rates of clinical failure and resistance.
- This study was to examine early clinical failure rates between patients receiving empiric third-generation cephalosporins or carbapenems for treatment of *Enterobacter* spp., *Serratia* spp., *Citrobacter* spp., or *Morganella morganii* infections (ESCPM pathogens).

Methods

Study Design and Population	• Retrospective chart review • Bloodstream and/or respiratory infections caused by ESCPM pathogens • 1:1 nearest neighbor propensity score matching of 30 matched pairs
Time Period	January 1, 2012 – June 1, 2020
Comparators	Third-generation cephalosporins versus carbapenems
Primary Outcome	Early Clinical Failure 48 to 72 hours after receipt of empiric antibiotics
Secondary Outcomes	• 30-day mortality • 30-day readmission • Repeat positive cultures • Susceptibility changes
Key sensitivity analyses	• Fisher's exact test (primary outcome) • Independent t-test (categorical variables) • 2-sided P values < 0.05 were considered statistically significant

Summary of Results

- Clinical failure that occurred 48 to 72 hours after receipt of empiric antibiotics was seen in 8 (26.7%) patients in the third-generation cephalosporin group and 9 (30%) patients in the carbapenem group (P = 1.00).
- Results for 30-day mortality, 30-day readmission, and susceptibility changes were not statistically significant between groups.
- Of the 19 patients in the third-generation cephalosporin group who received repeat cultures, 3 (10%) patients had positive cultures and of the 24 patients in the carbapenem group who received repeat cultures, 11 (36.7%) patients had positive cultures (P = 0.03).

Table 1. Clinical Outcomes by Therapy Group

Variable	Third-Generation Cephalosporins, n = 30	Carbapenem, n = 30	*P* Value
Clinical failure[a] , n (%)	8 (26.7)	9 (30.0)	1.00
Temperature >38°C	4 (13.3)	7 (23.3)	0.51
New mechanical ventilator	2 (6.7)	2 (6.7)	1.00
New vasopressor	2 (6.7)	2 (6.7)	1.00
Transfer to ICU	2 (6.7)	0 (0.0)	0.49
Death	0 (0.0)	0 (0.0)	
30-day mortality, n (%)	4 (13.3)	5 (16.7)	1.00
30-day readmission, n (%)	4 (13.3)	3 (10.0)	1.00
Infectious cause of 30-day readmission, n (%)	2 (6.7)	0 (0.0)	0.49

Table 2. Repeat Culture and Antibiotic Outcomes by Therapy Group

Variable	Third-Generation Cephalosporins, n = 30	Carbapenem, n = 30	*P* Value
Repeat culture, n (%)	19 (63.3)	24 (80.0)	0.25
Time to repeat culture, hours ± SD	46.2 ± 77.5	55.4 ± 76.7	0.64
Repeat culture positive, n (%)	3 (10.0)	11 (36.7)	0.03
Susceptibility changes, n (%)	1 (3.3)	1 (3.3)	1.00
Time from culture to antibiotic, hours ± SD	12.0 ± 22.2	18.9 ± 29.8	0.31
Empiric duration, hours ± SD	117.0 ± 89.5	195.7 ± 165.0	0.03

Conclusions

- This study suggests that third-generation cephalosporins are appropriate to use empirically in patients with infections due to *Enterobacter cloacae* complex, *Enterobacter aerogenes*, *Serratia* spp., *Citrobacter* spp., or *Morganella morganii*.
- Third-generation cephalosporins and carbapenems were comparable regarding clinical failure, 30-day mortality, and 30-day readmission.

Reference

Kamal, L.D., Kim, C., Archer, J., Dukes, J., Jeffres, M.N., Third-generation cephalosporins versus carbapenems for empiric treatment of *Enterobacter* spp., *Serratia* spp., *Citrobacter* spp., or *Morganella morganii* infections