Outcomes of Patients with Amp-C Inducible Enterobacteriaceae infections Treated with Carbapenems versus Cefepime or Piperacillin-tazobactam

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BACKGROUND

The CDC have recognized Enterobacteriaceae as an urgent threat causing up to 140,000 health care associated infections each year in the United States. There is a lack of data assessing the efficacy of different beta-lactam antibiotics for treatment of *Enterobacter* spp., *Serratia marcescens*, *Citrobacter freundii*, *Providencia* spp., and *Morganella morganii* (ESCPM) infections. These pathogens contain chromosomally located, inducible AmpC beta-lactamases, a unique mechanism of resistance. Limited data suggest that exposure to third-generation cephalosporins selects for AmpC-overproducing mutants and therefore are not recommended to treat ESCPM infections. Optimal therapy, beyond potentially avoiding third-generation cephalosporins, is unknown.

OBJECTIVES

- To compare clinical failure, 30-day mortality, and 30-day readmission rates between patients with ESCPM infections treated with a carbapenbem vs. cefepime or piperacillin/tazobactam

METHODS

Retrospective, multi-center, cohort study at an academic medical center and a Veterans Affairs hospital

- Inclusion criteria
  - Admitted between January 1, 2012 and January 1, 2015
  - Growth of an ESCPM pathogen from respiratory or blood culture
  - Empiric treatment with either CARB, CEF, or PT for at least 48 hours
  - Pathogen susceptible to empiric therapy
- Primary outcome – clinical failure
  - Assessed at 48 to 72 hours after receipt of empiric antibiotics and represented a composite of 1 or more of the following: temperature of ≥38.0C, need for new mechanical ventilation, increased or new need for vasopressor support, new admission to an intensive care unit, or death
- Secondary Outcomes: 30-day mortality, 30-day readmission
- Statistical analysis of primary outcome used 2-sided Fisher's exact test

RESULTS

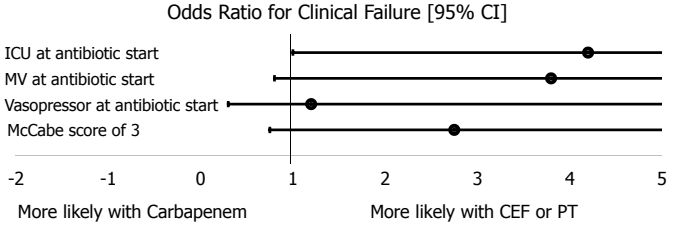
BASELINE CHARACTERISTICS

	Carbapenem, n=30	CEF or PT N=157	P value
Age, years ± SD	58.5 ± 12.6	58.1 ± 15.4	0.886
Male, n (%)	17 (56.7)	108 (68.8)	0.209
Caucasian, n (%)	20 (66.7)	95 (60.5)	0.378
Respiratory infection, n (%)	16 (53.3)	89 (56.7)	0.641
Bloodstream infection, n (%)	14 (46.7)	68 (43.3)	0.841
Immunosuppressed, n (%)	8 (26.7)	43 (27.4)	1.000
Diabetes, n (%)	12 (40.0)	51 (32.5)	0.527
COPD, n (%)	1 (3.3)	19 (12.1)	0.207
CKD on dialysis, n (%)	3 (10.0)	12 (7.6)	0.713
CHF, n (%)	4 (13.3)	20 (12.7)	1.000
Cirrhosis, n (%)	1 (3.3)	10 (6.4)	1.000
McCabe score of 3	21 (70.0)	105 (66.9)	0.834
E. cloacae, n (%)	16 (53.3)	73 (46.5)	0.552
E. aerogenes, n (%)	3 (10.0)	31 (19.7)	0.302
S. marcescens, n (%)	9 (30.0)	40 (25.5)	0.652
C. freundii, n (%)	2 (6.7)	10 (6.4)	1.000
Providencia spp., n (%)	0	2 (1.3)	1.000
M. morganii, n (%)	1 (3.3)	6 (3.8)	1.000
Severity of Illness at antibiotic start			
Intensive care unit, n (%)	22 (73.3)	115 (73.2)	1.000
Vasopressor use, n (%)	7 (23.2)	43 (27.4)	0.822
Mechanical ventilation, n (%)	17 (56.7)	83 (52.9)	0.842

OUTCOMES

	Carbapenem, n=30	CEF or PT N=157	P value
Clinical failure, n (%)	4 (13.3)	42 (26.8)	0.164
Fever at 48 hours, n (%)	3 (10.0)	25 (15.9)	0.578
New MV requirement, n (%)	2 (6.7)	7 (4.5)	0.638
New vasopressor use, n (%)	0	6 (3.8)	0.592
New ICU requirement, n (%)	0	2 (1.3)	1.000
Death at 48 hours, n (%)	1 (3.3)	9 (5.7)	1.000
30-day mortality, n (%)	7 (23.3)	39 (24.8)	1.000
30-day readmission, n/N (%)	2/23 (8.7)	21/118 (17.8)	0.368

CLINICAL FAILURE SUBGROUP ANALYSES



CONCLUSION

- The carbapenem group had numerically lower rates of clinical failure, mortality, and readmission. Results were not statistically significant.
- Patients in the ICU subgroup had higher rates of clinical failure when treated with cefepime or piperacillin/tazobactam (OR 4.2 95% CI 1.0-18.9) as compared to patients treated with a carbapenem. Other subgroups favored carbapenems but were not statistically significant.
- A study with a larger sample size would be needed to determine if the trend is significant in the overall patient population.

Disclosures: Authors of this presentation have no disclosures concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation

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