Piperacillin/tazobactam versus Cefepime for Empiric Treatment of *ampC* Producing *Enterobacteriaceae*

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Background

- The Centers for Disease Control and Prevention (CDC) reported 197,000 infections and 9,100 deaths caused by *Enterobacteriaceae* in 2017.[1]
- *AmpC* is a chromosomally inducible gene found in certain *Enterobacteriaceae*. When activated this causes the bacteria to produce beta-lactamase leading to antibiotic resistance and treatment failure with antibiotics unstable against ampC.[2,3]
- Though piperacillin/tazobactam is a weak inducer of ampC, the activation of the ampC gene can render the antibiotic to become resistant.[4]

Objective

Compare early clinical failure, 30-day mortality, and 30-day readmission between piperacillin/tazobactam and cefepime in patients with bloodstream and/or respiratory infections due to *Enterobacter cloacae* complex, *Klebsiella* (formerly *Enterobacter*) *aerogenes*, *Serratia* spp., *Citrobacter* spp., or *Morganella morganii* (ESCPM) infections.

Methods

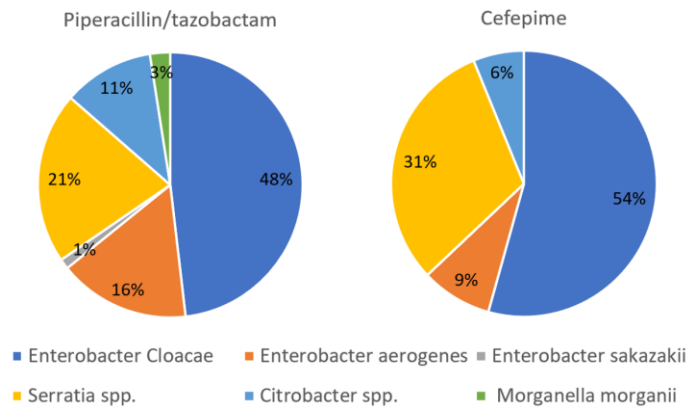
- 672 patient records were reviewed at the University of Colorado Hospital between January 1, 2012 and June 1, 2020.
- Patients with bloodstream and/or respiratory infection positive for ESCPM bacteria were included in the study. The ESCPM isolates must exhibit resistance to first-generation cephalosporin and sensitivity to third-generation cephalosporins, piperacillin/tazobactam, and carbapenems.
- 207 patients met inclusion criteria and after the 1:1 nearest neighbor propensity match pair analysis this yielded 81 matched pairs.
- Primary outcome: early clinical failure was assessed 48 to 72 hours after receipt of empiric antibiotics. Composite outcome defined objectively as either a temperature >38.0°C, new vasopressor, new mechanical ventilation, transfer to ICU, or death.

Results

Table 1. Baseline Characteristics

Patient Characteristics	Piperacillin/ tazobactam, n = 81	Cefepime, n = 81
Age, years ± SD	56 ± 16	57 ± 16
Male, n (%)	57 (70.4)	52 (64.2)
White/Caucasian, n (%)	50 (61.7)	57 (70.4)
Quick Pitt Score, mean ± SD	1.73 ± 1.2	1.80 ± 1.2
ICU admission, n (%)	50 (61.7)	44 (54.3)
Hospital origin, n (%)	28 (34.6)	38 (46.9)
Respiratory source, n (%)	38 (46.9)	29 (35.8)
Immunocompromised, n (%)	46 (56.8)	53 (65.4)
Repeat culture positive, n (%)	58 (71.6)	62 (76.5)
Empiric duration, hours ± SD	124.2 ± 82.2	146.4 ± 97.6

Figure 1. Organisms



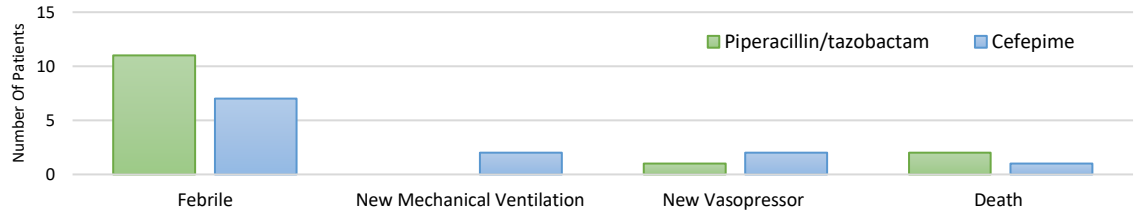
Results

162 Patients with bloodstream and/or respiratory infection due to **ESCPM** bacteria

	Piperacillin/tazobactam, n = 81	Cefepime, n = 81
Early Clinical Failure	14 (17.3%)	12 (14.8%)
	P value = .83	
30-day mortality	8 (9.9%)	12 (14.8%)
	P value = .47	
30-day readmission	14 (17.3%)	18 (22.2%)
	P value = .55	

No significant difference in early clinical failure, 30-day mortality, and 30-day readmission

Figure 2. Early Clinical Failure



Conclusion

- This study supports the use of piperacillin/tazobactam in patients with bloodstream and/or respiratory infections due to ESCPM bacteria. There was no statistical difference in early clinical failure, 30-day mortality, and 30-day readmission rates between piperacillin/tazobactam and cefepime therapy groups.
  - The use of piperacillin/tazobactam did not increase mortality or has worse clinical outcomes.
- Piperacillin/tazobactam can be safely used as an alternative treatment for *ampC* producing *Enterobacteriaceae*.
  - Piperacillin/tazobactam are weak inducers of *ampC* therefore, emerging resistance by induction or activation of *ampC* is relatively low and continued use of piperacillin/tazobactam empirically is appropriate.

References

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Piperacillin/tazobactam is **appropriate** to use empirically in patients with bloodstream and/or respiratory infections due to **ESCPM bacteria**