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.
- 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.
- Though piperacillin/tazobactam is a weak inducer of ampc, the activation of the ampc gene can render the antibiotic to become resistant.

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 sensitivity to third-generation cephalosporin and resistance to first-generation cephalosporins.
- 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 fever (temperature >38.0°C, new vasopressor, new mechanical ventilation, transfer to ICU, or death.

Results
Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Piperacillin/ tazobactam, n = 81</th>
<th>Cefepime, n = 81</th>
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</thead>
<tbody>
<tr>
<td>Age, years ± SD</td>
<td>56 ± 16</td>
<td>57 ± 16</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>57 (70.4)</td>
<td>52 (64.2)</td>
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<tr>
<td>White/Caucasian, n (%)</td>
<td>50 (61.7)</td>
<td>57 (70.4)</td>
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<td>Quick Pitt Score, mean ± SD</td>
<td>1.73 ± 1.2</td>
<td>1.80 ± 1.2</td>
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<tr>
<td>ICU admission, n (%)</td>
<td>50 (61.7)</td>
<td>44 (54.3)</td>
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<tr>
<td>Hospital origin, n (%)</td>
<td>28 (34.6)</td>
<td>38 (46.9)</td>
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<tr>
<td>Respiratory source, n (%)</td>
<td>38 (46.9)</td>
<td>29 (35.8)</td>
</tr>
<tr>
<td>Immunocompromised, n (%)</td>
<td>46 (56.8)</td>
<td>53 (65.4)</td>
</tr>
<tr>
<td>Repeat culture positive, n (%)</td>
<td>58 (71.6)</td>
<td>62 (76.5)</td>
</tr>
<tr>
<td>Empiric duration, hours ± SD</td>
<td>124.2 ± 82.2</td>
<td>146.4 ± 97.6</td>
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Figure 1. Organisms

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.

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

Piperacillin/tazobactam, n = 81
Cefepime, n = 81

Early Clinical Failure: 14 (17.3%) vs 12 (14.8%)
P value = .83

30-day mortality: 8 (9.9%) vs 12 (14.8%)
P value = .47

30-day readmission: 14 (17.3%) vs 18 (22.2%)
P value = .55

References

Contact/ Disclosure
Email: crystal.kim@cuanschutz.edu - The authors of this presentation report no conflict of interest and no funding.

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