Comparison of Glycopeptide or Lipopeptide versus Beta-Lactam for the Treatment of Enterococcus Faecalis Bacteremia: A National Retrospective Cohort Study of Veterans Affairs

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Disclosure

• The speaker has no actual or potential conflicts of interest in relation to this presentation
Project Background

• High incidence of 30-day all-cause mortality in enterococcal bacteremia (7-40%)

• Optimal therapy for Enterococcus faecalis (EF) has not been well studied

• Recent studies report mixed results comparing mortality risk of glycopeptide vs. beta-lactam therapy for enterococcal bacteremia

• No studies to date have compared outcomes for lipopeptides vs. beta-lactam or glycopeptide therapies for enterococcal bacteremia
## Previous Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Enterococcus Infection</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foo et al. 2014</td>
<td>172</td>
<td><strong>100% E. faecalis</strong></td>
<td>30-day all-cause mortality: 15%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(33% polymicrobial)</td>
<td>• Glycopeptide 26.1% vs. β-lactam 11.1% (<strong>p=0.015</strong>)</td>
</tr>
<tr>
<td>Fletcher et al. 2018</td>
<td>186</td>
<td><strong>95% E. faecalis</strong></td>
<td>30-day all-cause mortality: 7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(% polymicrobial not defined)</td>
<td>• Glycopeptide 6.7% vs. β-lactam 7.1% (<strong>p=0.922</strong>)</td>
</tr>
<tr>
<td>Petersiel et al. 2019</td>
<td>516</td>
<td><strong>77% E. faecalis</strong></td>
<td>30-day all-cause mortality: 40%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(38% polymicrobial)</td>
<td>• Glycopeptide 40.8% vs. β-lactam 39% (<strong>p=0.692</strong>)</td>
</tr>
</tbody>
</table>
Purpose

Study Objective

• To compare outcomes in patients with ampicillin-susceptible, vancomycin-susceptible *Enterococcus faecalis* bacteremia treated with intravenous glycopeptide, lipopeptide, or beta-lactam therapy
### Inclusion and Exclusion Criteria

#### Inclusion Criteria
- Patients age ≥18 years admitted to VAMC
- Clinically significant EF bacteremia
- EF susceptible to ampicillin (or penicillin) and vancomycin (daptomycin, if reported)
- Appropriate therapy with glycopeptide, lipopeptide, or beta-lactam antibiotic

#### Exclusion Criteria
- Subsequent episodes of EF bacteremia within the study period
- Treatment with combination of beta-lactam plus glycopeptide or lipopeptide
- Antibiotic therapy <5 days
- Polymicrobial bacteremia
Methods

• Retrospective review of national database of patients admitted to Veterans Affairs Medical Centers
  – January 1, 2012 to December 31, 2017

• Treatment Groups

<table>
<thead>
<tr>
<th>Beta-lactam Therapy</th>
<th>Glycopeptide Therapy</th>
<th>Lipopeptide Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Ampicillin</td>
<td>• Vancomycin</td>
<td>• Daptomycin</td>
</tr>
<tr>
<td>• Ampicillin/sulbactam</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VETERANS HEALTH ADMINISTRATION
End Points

• Primary
  – 30-day all-cause mortality

• Secondary
  – Recurrent *Enterococcus faecalis* bacteremia
  – Hospital mortality
  – One-year all-cause mortality
  – Incidence of *C. difficile* infection
  – Hospital and ICU length of stay
  – Duration of bacteremia

ICU, intensive care unit
Statistics

- **Power calculation**
  - 208 patients needed for 80% power to detect a 15% difference in 30-day all-cause mortality

<table>
<thead>
<tr>
<th>Primary Outcome</th>
<th>Type of Data</th>
<th>Statistical Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day all-cause mortality</td>
<td>Non-continuous</td>
<td>Fisher’s exact or Chi-squared</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kaplan-Meier with log-rank test</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary Outcomes</th>
<th>Type of Data</th>
<th>Statistical Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of recurrent bacteremia</td>
<td>Non-continuous</td>
<td>Fischer’s exact or Chi-squared</td>
</tr>
<tr>
<td>Incidence of C. difficile infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>One-year all-cause mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital and ICU length of stay</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of bacteremia</td>
<td>Continuous</td>
<td>T-test or Mann-Whitney U test</td>
</tr>
</tbody>
</table>
Results

1,038 unique patients hospitalized with *E. faecalis* bacteremia meeting study criteria

- **Ampicillin**  
  n = 112

- **Vancomycin**  
  n = 908

- **Daptomycin**  
  n = 18
## Patient Demographics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Ampicillin (n=112)</th>
<th>Vancomycin (n=908)</th>
<th>Daptomycin (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean years ± SD</td>
<td>72.7 ± 11.1</td>
<td>73.2 ± 11.5</td>
<td>72.4 ± 11.1</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>111 (99.1)</td>
<td>891 (98.1)</td>
<td>17 (94.4)</td>
</tr>
<tr>
<td>ICU admission location, n (%)</td>
<td>15 (13.4)</td>
<td>229 (25.2)</td>
<td>3 (16.7)</td>
</tr>
</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Ampicillin (n=112)</th>
<th>Vancomycin (n=908)</th>
<th>Daptomycin (n=18)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day all-cause mortality, n (%)</td>
<td>9 (8.0)</td>
<td>200 (22.0)</td>
<td>1 (5.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>1-year all-cause mortality, n (%)</td>
<td>38 (33.9)</td>
<td>448 (49.3)</td>
<td>6 (33.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>Hospital mortality, n (%)</td>
<td>5 (4.5)</td>
<td>138 (15.2)</td>
<td>1 (5.6)</td>
<td>0.005</td>
</tr>
</tbody>
</table>
Results

![Survival Rate Chart](chart.png)

- **Ampicillin**
- **Vancomycin**
- **Daptomycin**

Log-rank *P*=0.001
Results

![Graph showing percent survival over days for different antibiotics: Ampicillin, Vancomycin, and Daptomycin. The graph indicates log-rank P=0.002.](image)
Results

- Comparison of 30-day all-cause mortality between ampicillin and vancomycin treatment groups by multivariable logistic regression

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted Odds Ratio (95% confidence interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin treatment</td>
<td>2.80 (1.37-5.71)</td>
<td>0.005</td>
</tr>
<tr>
<td>ICU admission</td>
<td>3.68 (2.64-5.14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age</td>
<td>1.03 (1.01-1.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.36 (0.41-4.49)</td>
<td>0.617</td>
</tr>
</tbody>
</table>
Conclusion

• Vancomycin is associated with increased mortality compared to ampicillin for the treatment of clinically significant ampicillin-susceptible, vancomycin-susceptible *Enterococcus faecalis* bloodstream infection.

• Lowest mortality numerically observed in daptomycin group, but limited by power.
Future Directions

- Further collection and adjustment for confounding factors between groups
- Expansion of cohort years included to increase daptomycin sample
- Evaluation of effect of vancomycin dosing on outcomes
Limitations

• Retrospective study

• Limited data available at this time

• VA patient population
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References


Questions?

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