Background

- Carbapenem-resistance Enterobacteriaceae (CRE) - Highly drug resistant Gram negative bacteria - Can cause serious healthcare associated infections
- CDC Threat Level: Urgent

Methods

- Study Design: Retrospective chart review of all patients diagnosed with CRE on at least one clinical culture.
- Data collected from 1/1/2016 to 12/31/2016
- Hospital Setting: UCLA Health
- Fayeed Health UCLA Medical Center – tertiary referral center
- Santa Monica UCLA Medical Center – community hospital
- Inclusion criteria:
  - All patients with at least 1 clinical culture for CRE during study period
  - CRE = resistance to ertapenem, imipenem, or meropenem by broth microdilution
- Data Collection:
  - List of all patients with at least 1 clinical culture for CRE was obtained from the microbiology laboratory
  - Electronic health record charts were reviewed for demographic information, infection specific information, treatment information, and outcomes
- Analyses:
  - Primary outcome: Clinical success - defined as survival and absence of recurrence within 30 days from initial culture date, and resolution of signs/symptoms of infection and clearance of cultures within 7 days of treatment initiation - Secondary outcomes: 30 day mortality, recurrence and development of drug resistance - Statistics - chi square tests and logistic regression

Results

Demographics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>All Patients (n=279)</th>
<th>Percent/SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>173</td>
<td>61%</td>
</tr>
<tr>
<td>Female</td>
<td>106</td>
<td>39%</td>
</tr>
<tr>
<td>Race/Ethnicity:</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>84</td>
<td>30%</td>
</tr>
<tr>
<td>Black or African American</td>
<td>46</td>
<td>17%</td>
</tr>
<tr>
<td>Asian</td>
<td>13</td>
<td>4%</td>
</tr>
<tr>
<td>Native Hawaiian or Other Pacific Islander</td>
<td>8</td>
<td>3%</td>
</tr>
<tr>
<td>Other</td>
<td>26</td>
<td>9%</td>
</tr>
<tr>
<td>Declined</td>
<td>10</td>
<td>4%</td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>44</td>
<td>16%</td>
</tr>
<tr>
<td>Admitted from:</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>111</td>
<td>40%</td>
</tr>
<tr>
<td>Skilled Nursing Facility (SNF)</td>
<td>76</td>
<td>27%</td>
</tr>
<tr>
<td>Hospital</td>
<td>92</td>
<td>33%</td>
</tr>
<tr>
<td>Length of Stay (Days)</td>
<td>43.8</td>
<td>32.3</td>
</tr>
</tbody>
</table>
| Primary bacterium allergy | 25 | 9%
| ICU stay during hospitalization | 53 | 19%
| Presence of a central line | 69 | 25%
| Charlson Comorbidity Index | 6.6 | 32.1 |

Potential CRE Risk Factors

Presence of Risk Factors for CRE

Alcohol or EtOH use: 14%
Active drug or EtOH use: 21%
Diabetes or EtOH use: 21%
Hypertension or EtOH use: 20%
CHF or EtOH use: 16%
HIV or EtOH use: 12%
Liver disease or EtOH use: 11%
Cancer or EtOH use: 8%
Renal disease or EtOH use: 8%
COPD or EtOH use: 6%
Other: 4%
Unknown: 4%

Almost all patients were hospitalized within the last year
- At UCLA – 61%
- Outside Hospital – 39%

CRE Organisms

<table>
<thead>
<tr>
<th>microbiota</th>
<th>Organism</th>
<th>Percentage</th>
</tr>
</thead>
</table>
| Enterobacteriaceae | Klebsiella pneumoniae | 43%
| Enterococcus | Other | 23%

Mechanism of Resistance:

- KPC 33%
- NDM 1%
- OXA-48 3%
- VIM 1%
- Unknown 62%

Susceptibility Data

Susceptibility Data for All CRE Isolates

Comparison of Susceptibility Data in Patients with a Recurrence

<table>
<thead>
<tr>
<th>CRE Organism</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococcus</td>
<td>≤ 14%</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>≤ 12%</td>
</tr>
<tr>
<td>Enterobacter</td>
<td>≤ 15%</td>
</tr>
</tbody>
</table>

Outcomes

Reason for Clinical Failure

- Death within 30 days: 24%
- Ongoing signs or symptoms of infection at 30 days: 33%
- Ongoing positive cultures after 7 days: 17%
- CRE recurrence within 30 days: 4%

Risk Factors for Clinical Failure

Impact of Treatment on Clinical Success

<table>
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<tr>
<th>Patients with Adequate Source Control Had a Significantly Higher Likelihood of Clinical Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>cured</td>
</tr>
<tr>
<td>failed</td>
</tr>
</tbody>
</table>

Development of Ceftazidime-Avibactam Resistance with Therapy

- From initial isolates, only 3% were resistant to ceftazidime-avibactam
- One patient developed resistance after therapy:
  - 47 y.o. male with h/o HTN, EION, abuse, ESLD due hepatic hydrothorax, AKI on CVVHD, transferred from OSH for decompensated liver failure and renal failure, OLT listing, now with CRE pneumonia
  - After 10 days of treatment, had recurrent infection with Klebsiella pneumoniae
  - Ceftazidime-avibactam MIC increased from < 2 to 8 to 16 on repeat testing
  - Second isolate: Now susceptible to meropenem
  - Resistance mechanism: KPC2

Conclusions

- Despite newer agents to treat CRE infection, mortality, recurrence, and clinical failure remain high
- Source control remains a crucial part of treating CRE. There were no other treatments that led to improved outcomes
- Limitations: Single center study, small sample size, heterogeneous population, and wide variation in treatment strategies limit ability to determine factors leading to improved outcomes
- Next Steps: To collect additional CRE patient and outcomes data to increase the sample size and further determine factors leading to clinical success

References


Poster Board # 360

Carbapenem-resistant Enterobacteriaceae Associated with High Rates of Clinical Failure Despite Best Available Therapy

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