INTRODUCTION

- Carbapenems are broad-spectrum antibiotics that demonstrate time-dependent, bactericidal activity against both Gram-positive and Gram-negative pathogens.
  - The target pharmacodynamic index for carbapenems is a free drug concentration above the minimum inhibitory concentration (MIC) for approximately 40% of the dosing interval (~40/95 to MIC).
- Pharmacokinetic/pharmacodynamic (PK/PD) studies have demonstrated similar target attainment rates (~40/95 to MIC) between the conventional meropenem dosing strategy (1g IV every 8 hours) and an alternative dosing strategy (500mg IV every 6 hours).
- Differences in meropenem PK properties have been identified in obese patients.
- Clinical studies have demonstrated similar patient outcomes and increased cost savings with the alternative meropenem dosing strategy as compared with the traditional dosing approach.
- Limited clinical outcomes data are currently available comparing the two meropenem dosing strategies in obese patients.
- Given the rise in antimicrobial resistance and the prevalence of obesity in the United States, additional data are needed to confirm the clinical appropriateness of using carbapenem regimens that result in lower total daily doses.

OBJECTIVE

To compare clinical outcomes associated with two meropenem dosing strategies in an obese patient population.

METHODS

- Study Design:
  - Retrospective observational study
  - Two institutions within an university-affiliated academic health system: 535-bed and 520-bed community teaching hospitals
  - October 2011 – November 2014
- Inclusion Criteria
  - Adults (age 18 years or older)
  - Body mass index (BMI) of at least 30 kg/m²
  - Received meropenem therapy using one of the dosing strategies below for at least 3 consecutive days

<table>
<thead>
<tr>
<th>Meropenem Dosing Strategy</th>
<th>CeT &gt;30 mcg/ml</th>
<th>CeT 0-30 mcg/ml</th>
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</thead>
<tbody>
<tr>
<td>Traditional</td>
<td>1g IV q6h</td>
<td>1g IV q2h</td>
</tr>
<tr>
<td>Alternative</td>
<td>500mg IV q8h</td>
<td>500mg IV q6h</td>
</tr>
</tbody>
</table>

- Exclusion Criteria
  - Pregnancy
  - Creatinine clearance less than 30 mL/min and/or renal replacement therapy, any change in serum creatinine of greater than 0.5 mg/dL, or 50% above baseline after meropenem initiation
  - Meropenem use in previous 30 days
  - Cystic Fibrosis
  - Hematologic/oncology patients
  - Burn patients
  - Central nervous system infections
  - Admission to rehabilitation unit to finish meropenem treatment course

RESULTS

- Primary outcomes
  - Clinical response rate (defined as resolution of fever [Tmax < 38°C], normalization of WBC [<11,200 cells/mL], and resolution of infectious signs and symptoms at end of meropenem therapy or discharge (whichever came first)
    - Complete response: resolution of infectious signs and symptoms + fever resolution + normal WBC
    - Partial response: improving infectious signs and symptoms +/− fever resolution + normal WBC
    - Failed response: continued or worsening infectious signs and symptoms - fever resolution - normal WBC
  - Time to response (defined as resolution of fever [Tmax < 38°C] and normalization of WBC [<11,200 cells/mL])
    - Inclusion for this study outcome required presence of an abnormal WBC + fever to assess a response rate

- Secondary outcomes
  - Meropenem duration of therapy
  - In-hospital length of stay
  - In-hospital mortality

CONCLUSIONS AND LIMITATIONS

Limitations:
- Retrospective, single-center design with small sample size
- Differences between study groups

Conclusions:
- Results suggest that the similar clinical outcomes seen between traditional and alternative meropenem dosing strategies in previous studies may extend to the obese population
- Further research is needed to validate these findings

REFERENCES


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