A retrospective study to evaluate the use of nebulised meropenem at a large UK adult CF centre

V. Carrolan, E.F. Nash, R. Rashid, J.L. Whitehouse
West Midlands Adults Cystic Fibrosis Centre, Heart of England NHS Foundation Trust, Birmingham, UK

Background

- Cystic Fibrosis (CF) is the most common life-threatening inherited disease in Caucasians, affecting more than 9000 people in the UK [1].
- It is caused by dysfunction of the CF transmembrane conductance regulator (CFTR), an epithelial chloride channel essential for normal fluid movement across epithelial surfaces.
- The resultant thickened airway secretions result in chronic bacterial airway infection and progressive lung damage, with median life expectancy of 41 years [1].
- Pseudomonas aeruginosa is the most common bacterial pathogen affecting adults with CF, being associated with increased morbidity and more rapid decline in lung function.
- Meropenem is commonly used intravenously in CF patients infected with P. aeruginosa, but there is limited evidence of its tolerability and effectiveness when used as a nebulised treatment.

Aim

To evaluate the use of nebulised meropenem in our large UK adult CF centre

Methods

Medical records of CF patients who trialled nebulised meropenem between 2008-2012 were reviewed for: demographics, lung function, BMI, sputum microbiology, indications and tolerability and also number of exacerbations requiring intravenous (IV) antibiotics.

Results

Demographics
- 37 patients (18 male) trialled nebulised meropenem
  - Median age (IQR), 27 (20-37) years
  - Median FEV1% predicted (IQR), 48 (35-64)%
  - Median BMI (IQR), 23.1 (21.4-24.1) kg/m2
  - All patients were chronically infected with P. aeruginosa

Administration
- Patients received a 250 mg dose, reconstituted with 4ml water for injection, twice daily preceded by a bronchodilator

Indications
- Deteriorating condition or intolerance to other antibiotic nebulisers (21/37)
- Treatment of Burkholderia cepacia complex (BCC) (8/37)
- Treatment of non-tuberculous mycobacteria (8/37)

Tolerability
- 22/37 continue to tolerate nebulised meropenem.
- 10 of these 22 had previously been intolerant to Tobramycin Inhalation Solution (TIS) and 1 intolerant to nebulised amikacin.
- 4/37 discontinued due to no benefit or poor concordance
- 11/37 did not tolerate nebulised meropenem, reporting adverse effects including chest tightness, increased cough, chest discomfort, nausea and lethargy. 6 of these 11 had previously been intolerant to TIS and 2 were intolerant to amikacin.

Outcomes
- There were no significant changes in lung function, BMI or requirement for IV antibiotics comparing the 12-month period before and after commencing nebulised meropenem.
- However, CF patients with BCC appeared to benefit most in terms of courses of IV antibiotics and days in hospital compared to patients with other sputum microbiology (see Table 1).

<table>
<thead>
<tr>
<th></th>
<th>No of courses of IV 12/12 pre</th>
<th>No of courses of IVs 12/12 post</th>
<th>Days in hosp 12/12 pre</th>
<th>Days in hosp 12/12 post</th>
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</thead>
<tbody>
<tr>
<td>M. Abscessus</td>
<td>7</td>
<td>10</td>
<td>43</td>
<td>44</td>
</tr>
<tr>
<td>B. Cepacia</td>
<td>8</td>
<td>5</td>
<td>43</td>
<td>11</td>
</tr>
<tr>
<td>Other</td>
<td>23</td>
<td>25</td>
<td>211</td>
<td>293</td>
</tr>
</tbody>
</table>

Table 1. Courses of intravenous antibiotics and days in hospital pre and post-nebulised meropenem

Conclusion

Nebulised meropenem is generally well tolerated in CF adults and offers an alternative antibiotic choice for people with CF unable to tolerate other treatments.

References