Is Temocillin (TMO) combined with Amoxicillin (AMX) really an option for Hospital-Acquired Pneumonia (HAP)?

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• ↑ consumption of piperacillin/tazobactam (PIP/TAZ)
  o Correlated with an increase risk for resistant bacteria (Harris et al., AAC 2002, Lai et al., JAC 2011)
  ➢ need to conserve broad-spectrum antibiotics

• PIP/TAZ can induce C. difficile infection (CDI):
  o In our centre:
    ▪ 23 cases in 2010 (= 62% of all CDI cases)
    ▪ 17 cases in 2011 (= 71% of all CDI cases)
  o Other publications: Shah et al., JTACS 2012; Mendez et al., Pharmacotherapy 2006
AIMS OF THE STUDY

- Replace PIP/TAZ with temocillin + amoxicillin (TM+AMX) for treating severe Hospital Acquired Pneumonia (HAP)
  - Is it effective?
  - Is it safe (diarrhoea and C. difficile infection [CDI])?
- Temocillin was chosen because of
  - its narrow spectrum towards Gram negative
  - its stability against ESBL strains
  - the low prevalence of CDI reported
- The combination TMO+AMX was only possible because of the low incidence of P. aeruginosa in our centre
WHAT IS TEMOCILLIN?

- A Penicillin (6-α-methoxy derivative of ticarcillin)
- Narrow spectrum:
  - Gram negative only, except *Pseudomonas, Acinetobacter, Stenotrophomonas*
- Stable to most types of β-lactamases:
  - Including most AmpCs and ESBLs
- Licensed in BE, LUX and UK:
  - Septicaemia/bacteraemia
  - Urinary tract infection
  - Lower respiratory tract infection
# HOSPITAL GUIDELINES

<table>
<thead>
<tr>
<th>HAP</th>
<th>PREVIOUS</th>
<th>NEW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild/moderate</td>
<td>Doxycycline</td>
<td>Doxycycline</td>
</tr>
<tr>
<td>Severe</td>
<td>PIP/TAZ</td>
<td>TMO + AMX (teicoplanin instead of AMX if MRSA)</td>
</tr>
<tr>
<td>Aspiration pneumoniae</td>
<td>PIP/TAZ</td>
<td>TMO + AMX + metronidazole</td>
</tr>
</tbody>
</table>

**PIP/TAZ:** 4g/0.5g TDS (adjust dose in renal failure) - **AMX:** 1g TDS - **TMO** 2g BD (adjust dose in renal failure)
STUDY DESIGN

- Retrospective data collection from Clinical Coding Department
  - Between January 2011 and July 2012
- Patients with severe HAP only
  - new or persistent otherwise unexplained infiltrates on chest X-ray
  - increased oxygen requirements
  - temperature <36°C or > 38.4°C
  - CURB-65 score > 2
- Empirically treated with PIP/TAZ or TMO+AMX for at least 3 days
- Exclusion of patients with penicillin allergy and patients receiving other combination of antibiotics
247 patients reviewed, 49 were excluded

<table>
<thead>
<tr>
<th></th>
<th>PIP/TAZ (n=99)</th>
<th>TMO+AMX (n=99)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>40/59</td>
<td>49/50</td>
<td>NS</td>
</tr>
<tr>
<td>Age (year [mean±SD])</td>
<td>79.2 ± 12.5</td>
<td>79.7 ± 13.7</td>
<td>NS</td>
</tr>
<tr>
<td>Treatment duration (days [mean±SD])</td>
<td>6.7 ± 1.6</td>
<td>6.8 ± 1.5</td>
<td>NS</td>
</tr>
<tr>
<td>Prior antibiotic (n)</td>
<td>47</td>
<td>47</td>
<td>NS</td>
</tr>
<tr>
<td>Hosp. time (days [mean±SD])</td>
<td>29.7 ± 21</td>
<td>27.9 ± 18.5</td>
<td>NS</td>
</tr>
<tr>
<td>Concomitant antibiotic (n)</td>
<td>8</td>
<td>10</td>
<td>NS</td>
</tr>
<tr>
<td>Lung Injury Prediction Score</td>
<td>4.99 ± 2.0</td>
<td>5.02 ± 1.9</td>
<td>NS</td>
</tr>
<tr>
<td>ALI/ARDS (n)</td>
<td>17</td>
<td>14</td>
<td>NS</td>
</tr>
</tbody>
</table>
**RESULTS**

Microbiology - Respiratory Tract/Blood Culture

<table>
<thead>
<tr>
<th></th>
<th>PIP/TAZ (n=99)</th>
<th>TMO+AMX (n=99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram positive</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td><em>Pseudomonas</em></td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Yeasts</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Not reported</td>
<td>86</td>
<td>89</td>
</tr>
</tbody>
</table>

Difficulties of elderly patients to produce enough sputum to get a specimen for cultures 50% of our patients received previous antibiotic treatment
**CLINICAL EFFICACY**

Differences are not statistically different
DIARRHOEA AND CDI

Significant diarrhoea = type 6 or 7 Bristol stool chart

- PIP/TAZ: 34% significant diarrhoea, 8% CDI
  - P < 0.0001

- TMO+AMX: 4% significant diarrhoea, 0% CDI
  - P = 0.0067
ECONOMICAL BENEFITS?

Hospitalisation time (days)

Diarrhoea +: 38
Diarrhoea -: 27

P < 0.005

Hospitalisation time (days)

CDI +: 49
CDI -: 29

P = 0.0077
CONCLUSIONS

In a centre with low incidence of *Pseudomonas aeruginosa*:

• The combination of Temocillin with Amoxicillin could be a therapeutic option for treatment of severe HAP and is associated with a better safety profile as it induces **significantly fewer** cases of diarrhoea and of *C. difficile* infection

• Since the introduction of our guidelines:
  
  - 30% of PIP/TAZ consumption
  - Decrease of CDI associated with PIP/TAZ:
    ▪ 6 cases in 2012 (= 42% of all CDI cases)
    ▪ 17 cases in 2011 (= 71% of all CDI cases)
    ▪ 23 cases in 2010 (= 62% of all CDI cases)
• Dr B. Sajin & Dr K. Patel (Ashford & St. Peter’s Hospitals)

• Dr C. Grundy (Ashford & St. Peter’s Hospitals)

• Dr S. Van de Velde

• Dr A. Al-Dujaili