Antibiotic resistance in a collection of *Pseudomonas aeruginosa* isolated from Cystic Fibrosis patients through Europe (Belgium, France, Germany and United Kingdom)

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**Abstract**

Cystic fibrosis (CF) is the most common life-limiting disease in NW European populations. The primary cause of death in CF patients is the progressive lung disease mainly caused by chronic and recurrent bacterial infections, especially caused by *Pseudomonas aeruginosa*. Here we evaluated the activity of different classes of antibiotics against *Pseudomonas aeruginosa* isolates collected from CF patients in 4 CF centres across Europe. We found that colistin is the most active agent against this collection (often used as last-resort antibiotic), followed by tobramycin and meropenem. The resistance rates to the other main antipseudomonal agents are worryingly high.

**Objectives**

Our aim was to determine MIC distributions and resistance rates to major antipseudomonal antibiotics against isolates collected from CF patients in 4 centers through Europe.

**Materials & Methods**

Bacterial isolates: 342 *P. aeruginosa* isolates were collected in 4 Cystic Fibrosis centers from different countries (Hôpital des enfants malades Reine Fabiola/Erasme; Belgium, n = 91; Hôpital Jean Minjoz, Besançon, France; n = 81; University Hospital of Münster, n = 71, Germany; Queen’s; University of Belfast, UK, n=99).

Susceptibility testing: Minimal Inhibitory Concentrations (MIC) were determined by microdilution in cation-adjusted Mueller-Hinton broth following CLSI recommendations, with P.a. ATCC 27853 used as quality control strain. Susceptibility was assessed according to The European Committee on Antimicrobial Susceptibility Testing (EUCAST) interpretive criteria (2).

Analysis of cross resistance: This was assessed using quantile density contour analysis (QDC; 0.1 to 0.9) using JMP software v10.0.2

**Results**

Table 1: MIC distributions and percentage of susceptibility/resistance based on EUCAST breakpoints

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>AMK</th>
<th>TOB</th>
<th>CIP</th>
<th>CST</th>
<th>MEM</th>
<th>TZP</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIC (mg/L)</td>
<td>0.25</td>
<td>0.5</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Susceptible</td>
<td>&gt;512</td>
<td>64</td>
<td>&gt;128</td>
<td>&gt;512</td>
<td>&gt;512</td>
<td>&gt;512</td>
</tr>
<tr>
<td>Resistant</td>
<td>8</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 2: Percentage of cross resistance among tested antibiotics

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>AMK</th>
<th>TOB</th>
<th>CIP</th>
<th>CST</th>
<th>MEM</th>
<th>TZP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistence</td>
<td>AMK</td>
<td>TOB</td>
<td>CIP</td>
<td>CST</td>
<td>MEM</td>
<td>TZP</td>
</tr>
<tr>
<td>Percentage</td>
<td>3%</td>
<td>4%</td>
<td>2%</td>
<td>1%</td>
<td>2%</td>
<td>1%</td>
</tr>
</tbody>
</table>

**Background**

Cystic fibrosis (CF) is an autosomal recessive genetic disease, affecting mainly NW European populations and characterized by overproduction of sticky, thick mucus in many organs such as the lung, pancreas and gastrointestinal tract. This offers an ideal environment in the lung for proliferation of opportunistic pathogens. *Pseudomonas aeruginosa* is the most common micro-organism causing chronic respiratory tract infections in CF patients older than 25 years (1). These patients, therefore, require repeated and prolonged antibiotic treatments with anti-pseudomonal drugs. If effective, these treatments contribute to increasing life expectancy and maintaining a acceptable quality of life. Antibiotics belonging to the classes of β-lactams, aminoglycosides, fluoroquinolones and polymyxins (the latter as last-resort antibiotics) are used to treat pseudomonal infections.

**Conclusions**

- More than half of the isolates were resistant to amikacin, cefazidime, piperacillin-tazobactam, and ciprofloxacin, 20-25 % to tobramycin and meropenem, and only 7 % to colistin (which appears as a last-resort antibiotic).
- Cross-resistance was rare with colistin, 26 % among aminoglycosides, 18-62 % among β-lactams, and 35-44 % among drugs from different classes with high resistance rates (CIP, TZP, CAZ, AMK).
- Among aminoglycosides, tobramycin appears more active than amikacin, most probably due to the high prevalence antibiotic usage in the corresponding population, with best options remaining colistin, meropenem, and, if needed, colistin.
- High concentrations at the infection site are therefore required to reach pharmacodynamic target and inhaled formulations may prove a useful strategy in this context.

**References**

2. http://www.eucast.org (Clinical breakpoints)
5. TOB Posthalell prescribing information; Novartis; last update: March 2013

A copy of this poster will be made available after the meeting at http://www.facm.ucl.ac.be/posters.htm