In Vitro Comparison of Kanamycin, Kanendomycin, Gentamicin, Amikacin, Sisomicin, and Dibekacin Against 200 Strains of Pseudomonas aeruginosa

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The antimicrobial activity of kanamycin, kanendomycin, gentamicin, amikacin, sisomicin, and dibekacin against 200 strains of Pseudomonas aeruginosa was compared. Dibekacin was found to be the most active against the tested organisms, whereas the other aminoglycoside antibiotics fell in the following order of diminishing antibacterial potency: amikacin, sisomicin, gentamicin, kanendomycin, and kanamycin. Seven strains showed high-level resistance to gentamicin (minimal inhibitory concentration, 400 μg/ml), and two of them were also resistant to amikacin and sisomicin (minimal inhibitory concentration, 75 μg/ml). The minimal inhibitory concentration of dibekacin for these seven strains was 0.625 μg/ml.

This study was carried out to compare the in vitro antibacterial activity of six aminoglycoside antibiotics, kanamycin, kanendomycin, gentamicin, amikacin, sisomicin, and dibekacin, against 200 strains of Pseudomonas aeruginosa of an overnight culture in nutrient broth, containing approximately $10^6$ colony-forming units. A medium control with no antibiotic added was provided for each organism tested to assure viability, and medium controls with no antibiotic were also used to assure sterility of the medium. The MICs were expressed as the lowest concentration of antibiotic that totally inhibited visible growth after incubation for 24 h at 37°C. All the MICs mentioned in the text are expressed in the terms of aminoglycoside base of the antibiotics.

The MICs of the six aminoglycoside antibiotics mentioned above are illustrated in Table 1. Figure 1 shows the relationship between MICs and cumulative percentages of strains inhibited.

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**Table 1. MICs of six aminoglycoside antibiotics against 200 strains of P. aeruginosa**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>10</th>
<th>5</th>
<th>2.5</th>
<th>1.25</th>
<th>0.625</th>
<th>0.312</th>
<th>0.156</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dibekacin</td>
<td>4</td>
<td>13</td>
<td>23</td>
<td>45</td>
<td>66</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>Kanamycin</td>
<td>47</td>
<td>32</td>
<td>29</td>
<td>14</td>
<td>6</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Kanendomycin</td>
<td>60</td>
<td>28</td>
<td>30</td>
<td>16</td>
<td>11</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>30</td>
<td>32</td>
<td>51</td>
<td>40</td>
<td>26</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>4</td>
<td>19</td>
<td>41</td>
<td>59</td>
<td>35</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Sisomicin</td>
<td>20</td>
<td>35</td>
<td>54</td>
<td>42</td>
<td>29</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

* MIC for 63 strains was >100 μg/ml.
* MIC for 45 strains was >100 μg/ml.
* MIC for seven strains was 400 μg/ml.
* MIC for two strains was 75 μg/ml.

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isolated from hospitalized patients and against one control strain, P. aeruginosa ATCC 2753. The strains of P. aeruginosa were identified in accordance with Cowan and Steel's Manual for the Identification of Medical Bacteria (1).

Minimal inhibitory concentrations (MICs) were determined by using a serial dilution method of antibiotic assay in nutrient broth (Difco Laboratories) unmodified, i.e., with no added calcium or magnesium. The inoculum of the tested strains was 0.1 ml of a suitable dilution and no organism were also used to assure sterility of the medium. The MICs were expressed as the lowest concentration of antibiotic that totally inhibited visible growth after incubation for 24 h at 37°C. All the MICs mentioned in the text are expressed in the terms of aminoglycoside base of the antibiotics.

The MICs of the six aminoglycoside antibiotics mentioned above are illustrated in Table 1. Figure 1 shows the relationship between MICs and cumulative percentages of strains inhibited.
All strains tested were very susceptible to dibekacin; the MICs for 200 strains ranged from 0.156 to 2.5 μg/ml, and the MIC was 5 μg/ml for only four strains. In contrast, seven strains showed high-level resistance to gentamicin (MIC, 400 μg/ml), and two of the seven were also resistant to amikacin and sisomicin (MIC, 75 μg/ml). The MIC of dibekacin for these seven strains was 0.625 μg/ml.

At an MIC higher than 5 μg/ml, we found 55, 52, 18, 3, and 11% of the 200 strains tested resistant to kanamycin, kanendomycin, gentamicin, amikacin, and sisomicin, respectively. High-level resistance was defined as an MIC above 75 μg/ml, and on this basis 31, 22, 4, 1, and 1% of the strains were highly resistant to kanamycin, kanendomycin, gentamicin, amikacin, and sisomicin, respectively. *P. aeruginosa* strains resistant to high concentrations of amikacin and sisomicin were isolated for the first time in Greece, and this is important because sisomicin has not been introduced yet in Greece, and amikacin has been introduced only recently.

In conclusion, susceptibility tests of 200 strains of *P. aeruginosa*, all clinical isolates, showed that dibekacin (3',4'-dideoxykanamycin B), which was derived from kanamycin B by chemical transformation (2), has potent antimicrobial activity that is also exerted against *P. aeruginosa* strains that are resistant to high concentrations of gentamicin, amikacin, and sisomicin.

**LITERATURE CITED**