In Vitro Activity of Ceftriaxone Alone and in Combination with Gentamicin, Tobramycin, and Amikacin Against 

*Pseudomonas aeruginosa*

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Ceftriaxone, a new third-generation cephalosporin with a very long serum half-life, has been shown to have a wide antimicrobial spectrum. Its activity against *Pseudomonas aeruginosa*, however, is rather limited (1, 5, 6, 8). The in vitro activity of ceftriaxone against 50 *P. aeruginosa* strains was studied by the broth dilution method and the time-kill curve method. The majority of the *P. aeruginosa* strains tested were resistant to ceftriaxone. Combining ceftriaxone with the aminoglycosides resulted in synergism, antagonism, or indifference.

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Ceftriaxone is a third-generation cephalosporin with a very long serum half-life, and it has been shown to have a wide antimicrobial spectrum. Its activity against *Pseudomonas aeruginosa* is limited (1, 5, 6, 8). The study of ceftriaxone against 50 *P. aeruginosa* strains was performed using the broth dilution method and the time-kill curve method. The majority of the *P. aeruginosa* strains were resistant to ceftriaxone. Combining ceftriaxone with aminoglycosides resulted in synergism, antagonism, or indifference.

The study evaluated the in vitro activity of ceftriaxone alone and in combination with gentamicin, tobramycin, and amikacin against 50 *P. aeruginosa* strains using the broth dilution method and the time-kill curve method. The majority of the strains tested were resistant to ceftriaxone. Combining ceftriaxone with aminoglycosides led to synergistic, antagonistic, or indifferent effects.

### TABLE 1. In vitro susceptibilities of 50 *P. aeruginosa* strains

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC/MBC (μg/ml)</th>
<th>50%</th>
<th>90%a</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin</td>
<td>2/16</td>
<td>4/32</td>
<td>1-&gt;64/2-&gt;64</td>
<td></td>
</tr>
<tr>
<td>Tobramycin</td>
<td>1/2</td>
<td>2/8</td>
<td>0.125-&gt;64/0.5-&gt;64</td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>2/8</td>
<td>8/32</td>
<td>1-32/2-32</td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>&gt;64/2&gt;64</td>
<td>&gt;64/2-&gt;64</td>
<td>4-&gt;64/64</td>
<td></td>
</tr>
</tbody>
</table>

* MIC/MBC for 50% of strains.  
* MIC/MBC for 90% of strains.
that of both drugs alone at a given time, it was defined as synergism. When the result of the combination was at least a $2 \times \log_{10}$ increase in viable CFU from that of either drug alone, it was defined as antagonism. Results of the MIC and MBC determinations are shown in Table 1. The majority of the $P. aeuruginosa$ strains were resistant to ceftriaxone, confirming previous reports (1, 5, 6, 8). Using a method that employs an inoculum ($10^6$ CFU/ml) and a subculture volume (0.01 ml) sufficient to allow accurate determination of the MBC (7), we found that an MBC/MIC ratio of $\geq 4$ for ceftriaxone was common among the susceptible strains. The results of time-kill curve studies are shown in Table 2. Both synergism and antagonism were shown, although indifference was shown for the majority of strains. Neu et al. reported that the combination of ceftriaxone and gentamicin demonstrated synergistic inhibitory activity against one of five $P. aeuruginosa$ strains tested (6). Fass reported synergistic inhibitory activity of ceftriaxone and tobramycin in combination against 73% of 52 $P. aeuruginosa$ strains tested by the checkerboard microtube method (3). Antagonism was not mentioned by Neu et al. or Fass (3, 6). Antagonism was not found in two other studies in which combinations of aminoglycosides and other new cephalosporins were used (4, 9).

Using the time-kill curve method with a sufficient inoculum size ($10^6$ CFU/ml), we demonstrated both synergism and antagonism between ceftriaxone and an aminoglycoside against $P. aeuruginosa$. Since the effects of such combinations are unpredictable and strain dependent (9), its clinical use against $P. aeuruginosa$ infections requires further careful prospective clinical investigation.

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LITERATURE CITED