Combination antibiotic therapy is often indicated for health care-associated pneumonia due to resistant pathogens and is recommended in the Infectious Diseases Society of America/American Thoracic Society guidelines on the management of community-acquired pneumonia and health care-associated pneumonia (1, 4). Antibiotic aerosolization enhances delivery to the lower respiratory tract while theoretically limiting toxicity. Aerosolized tobramycin (TOBI) is currently approved for use only in patients with cystic fibrosis (CF). According to the manufacturer (2007 tobramycin inhalation solution USP prescribing information, Novartis Pharmaceuticals, East Hanover, NJ), patients with normal renal function do not require routine tobramycin concentration monitoring. However, there is limited evidence of the safety of the use of TOBI in the non-CF population. Brown et al. found TOBI to be safe and to result in a microbiologic cure, but clinical outcomes did not differ from those achieved with systemic therapy (2). Systemic absorption of 40 mg TOBI every 8 h resulted in detectable levels but did not affect renal function. In our safety study, we postulated that non-CF patients would have similar serum tobramycin concentrations and that patients with normal renal function would not have tobramycin-associated renal insufficiency.

The Institutional Review Board of Miami Valley Hospital (MVH) approved this study. Located in Dayton, OH, MVH is an 848-bed level 1 trauma center with 69 intensive care unit beds. MVH is a community teaching hospital affiliated with the Wright State University Boonshoft School of Medicine.

We conducted a prospective, open-label study of medical, surgical, and trauma patients who were prescribed TOBI by their treating physicians. TOBI was administered via a standard nebulizer over 30 min. To ensure maximum delivery of the drug and to minimize oropharyngeal binding, only patients with either an endotracheal tube or a tracheotomy were included. Dosing was 300 mg of TOBI every 12 h; the primary physician determined the duration of treatment. Exclusion criteria included concomitant use of macrolide antibiotics, as this would enhance binding to respiratory mucosa, and renal function would not have tobramycin-associated renal insufficiency.

TABLE 1. Serum tobramycin concentrations and creatinine levels of patients treated with 300 mg TOBI every 12 h

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Duration of treatment (days)</th>
<th>Serum tobramycin concen (g/ml)</th>
<th>Glomerular filtration rate (creatinine level [mg/dl])</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Before treatment</td>
</tr>
<tr>
<td>1</td>
<td>8</td>
<td>&lt;0.50*</td>
<td>&gt;70 (0.2)</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>&lt;0.50*</td>
<td>&gt;70 (0.6)</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>&lt;0.50*</td>
<td>&gt;70 (0.5)</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>0.80†</td>
<td>45 (1.5)</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>&lt;0.50*</td>
<td>&gt;70 (0.5)</td>
</tr>
<tr>
<td>6</td>
<td>12</td>
<td>&lt;0.50*</td>
<td>&gt;70 (0.5)</td>
</tr>
<tr>
<td>7</td>
<td>7</td>
<td>&lt;0.50*</td>
<td>&gt;70 (0.6)</td>
</tr>
<tr>
<td>8</td>
<td>12</td>
<td>&lt;0.50*</td>
<td>31 (1.6)</td>
</tr>
<tr>
<td>9</td>
<td>8</td>
<td>&lt;0.50*</td>
<td>&gt;70 (0.2)</td>
</tr>
</tbody>
</table>

* Two serum drug levels obtained on days 4 and 8.
† Three serum drug levels obtained on days 8 and 12.
‡ Serum drug level obtained on day 4.

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REFERENCES


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