In Vitro Susceptibility of *Mycobacterium fortuitum* and *Mycobacterium chelonei* to Cefmetazole

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The in vitro susceptibility of *Mycobacterium fortuitum* and *Mycobacterium chelonei* to cefmetazole was studied by the agar dilution method. At a concentration of 16 μg/ml or lower, 44 isolates (96%) of *M. fortuitum* and 8 isolates (40%) of *M. chelonei* were inhibited.

Infections caused by atypical mycobacteria, especially those of nosocomial origin, appear to be observed more frequently than in the past. This is particularly true of such rapidly growing mycobacteria as *Mycobacterium fortuitum* and *Mycobacterium chelonei*, which have been associated with such human infections as lung disease, subcutaneous abscess, thyroiditis, corneal ulcer, osteomyelitis, septicemia, meningitis, cervical adenitis, and urinary tract infections (9, 16).

The major problem with infections caused by rapidly growing mycobacteria is not their diagnosis, which can be accomplished quite simply (11), but rather their treatment. Both *M. fortuitum* and *M. chelonei* are very resistant to most antituberculosis agents (10).

Although in vitro activity of such antimicrobial agents as amikacin, doxycycline, sulfonamides, and erythromycin against the *M. fortuitum* complex has been reported (4, 7, 8, 13, 15), there is little agreement regarding the therapeutic effectiveness of these agents. Therefore, persons infected with these rapidly growing mycobacteria commonly are treated individually, depending on the antimicrobial agents to which the isolated organism is susceptible. The β-lactam antibiotics have been shown to be ineffective against *M. fortuitum* and *M. chelonei* in vitro (1); however, recent reports have indicated that cefoxitin is active against *M. fortuitum* (3, 6), but less so against *M. chelonei*. In this study we investigated the MICs of another cephamycin, cefmetazole, against *M. fortuitum* and *M. chelonei*.

Isolates of *M. fortuitum* and *M. chelonei* were provided by the American Type Culture Collection, Rockville, Md., and The National Collection of Type Cultures, London, England. Additional isolates were from our own laboratory and the following individual collections: L. Eidus and A. Laszlo, Laboratory Centre for Disease Control, Ottawa, Ontario, Canada; R. Gordon, Rutgers University, New Brunswick, N.J.; P. A. Jenkins, Tuberculosis Reference Laboratory, Cardiff, Wales; J. Viallier, Hospital J. Courmont, P. Benite, Lyon, France; I. Tarnok, Forschungsinstitut, Borstel, Germany; H. David, Institut Pasteur, Paris, France; G. Sabater, Hospital Militar, Valencia, Spain; H. Saito, Shimane Medical University, izumo, Japan; and E. Mankiewicz, Montreal, Quebec, Canada.

The identification of *M. fortuitum* and *M. chelonei* was confirmed on the basis of nitrate reduction (12), iron uptake (14), and susceptibility to pipemidic acid (2). *Staphylococcus aureus* ATCC 25923 (Difco Laboratories, Detroit, Mich.) was used as a control organism. Cefmetazole was supplied by Antibiotics S.A., Madrid, Spain.

Mycobacteria for susceptibility testing were grown for 7 days at 28°C on Dubos oleic agar base (Difco). Aqueous suspensions of the cultures were prepared and diluted with distilled water to a final concentration of about 10⁶ CFU/ml. In each experiment, the initial concentration of organisms was determined by titration and plating in duplicate.

Agar dilution testing was performed with Mueller-Hinton agar (Difco). After autoclaving, the agar was cooled to 56°C before the addition of cefmetazole to final concentrations that ranged from 0.25 to 128 μg/ml. The agar containing cefmetazole was poured into plates and allowed to solidify overnight. The plates were inoculated with 0.001 ml per spot with a Steers replicator.

Plates inoculated with *S. aureus* and *M. fortuitum* were incubated at 37°C and examined after 24 and 72 h, respectively. Plates inoculated with *M. chelonei* were examined after 72 h of incubation at 28°C. The MIC was considered as the lowest concentration that completely inhibited visible bacterial growth.

The MIC of cefmetazole for *M. fortuitum* was generally lower than that for *M. chelonei* (Table 1). A total of 44 (96%) of the 46 strains of *M. fortuitum* but only 8 (40%) of the 20 strains of *M. chelonei* were inhibited by a drug concentration of 16 μg/ml or less. Agar dilution MICs for 38 isolates (83%) of *M. fortuitum* were 8 μg/ml or less. Agar dilution MICs for 2 isolates (10%) of *M. chelonei* were more than 128 μg/ml.

Since parenteral doses of 0.25 and 0.5 g of cefmetazole yield serum levels of 20.5 and 32.5 μg/ml, respectively, it would appear that many strains of *M. fortuitum* and a few strains of *M. chelonei* might be inhibited by low doses of this drug. The activity of cefmetazole was greater than that reported for cefoxitin (3, 5, 6).

Previous studies have shown the following β-lactam antibiotics to be inactive against *M. fortuitum*: ampicillin, carbenicillin, cloxacillin, methicillin, nafcillin, oxacillin, penicillin, cephalothin, cephaloridine, cefamandole, and cephalaxin (1). Imipenem has recently been found to be active against *M. fortuitum* (5). Other agents which may be active against *M. fortuitum* and *M. chelonei* are erythromycin and tetracycline.

The encouraging in vitro results obtained with cefmetazole require substantiation in animal studies and clinical trials in humans. As in the treatment of tuberculosis, however, it seems likely that mycobacterioses due to rapid growers will continue to require treatment with several antimicrobial agents.
TABLE 1. Activity of cefmetazole against *M. fortuitum* and *M. chelonei* as determined by dilution testing

<table>
<thead>
<tr>
<th>Species</th>
<th>No. of strains</th>
<th>MIC (µg/ml)*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Range 50% 90%</td>
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<tr>
<td><em>M. fortuitum</em></td>
<td>46</td>
<td>4-64 6.4 12</td>
</tr>
<tr>
<td><em>M. chelonei</em></td>
<td>20</td>
<td>8-&gt;128 23.7 &gt;128</td>
</tr>
</tbody>
</table>

* MACs required to inhibit 50 and 90% of the strains, respectively.

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LITERATURE CITED