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 cephemycin, 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. Eids 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 pipemic 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 10⁵ 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, cefoxitin, methicillin, nafcillin, oxacillin, penicillin, cephalothin, cephaloridine, cefamandole, and cephalixin (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 mycobacteriose 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>
</tr>
</thead>
<tbody>
<tr>
<td>M. fortuitum</td>
<td>46</td>
<td>4–64</td>
</tr>
<tr>
<td>M. chelonei</td>
<td>20</td>
<td>8–&gt;128</td>
</tr>
</tbody>
</table>

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

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LITERATURE CITED