In Vitro Activity of Midecamycin, a New Macrolide Antibiotic

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Midecamycin, an acetoxy-substituted macrolide antibiotic, was tested against gram-positive and gram-negative bacteria. It inhibited the majority of streptococci, staphylococci, and strains of Haemophilus and Listeria at concentrations of <3.1 μg/ml. It was less active than erythromycin, and it failed to inhibit erythromycin-resistant isolates.

Interest in macrolide antibiotics has been rekindled by the new uses of the erythromycin for treatment of infections due to organisms such as Legionella spp. and Campylobacter spp. Erythromycin has a long history of successful use as an alternative to penicillin against many gram-positive bacteria. However, it does produce significant gastrointestinal discomfort in many adults. Midecamycin (Fig. 1) is a macrolide in which an acetoxy group is substituted on position 9 of the 16-member ring and on position 4 of the terminal sugar. It has been reported to act against some erythromycin- and josamycin-resistant bacteria (1). Midecamycin is alleged to have no bitter taste, and it can be administered orally with good absorption (1).

Midecamycin was a gift from the Central Research Laboratories of Meiji Seika Kaisha Ltd., Yokohama, Japan. Erythromycin was supplied by Abbott Laboratories, North Chicago, Ill. Methicillin and ampicillin were provided by Beecham Laboratories, Bristol, Tenn., and vancomycin was supplied by Lilly Research Laboratories, Indianapolis, Ind. All organisms had been cultured from patients hospitalized at the Columbia-Presbyterian Medical Center, New York, N.Y. Organisms had been identified by standard methods. Minimal inhibitory concentrations (MICs) of staphylococci and gram-negative species were determined with Mueller-Hinton agar by the spot inoculum method with an inoculum of 10⁵ CFU. MICs of streptococci and Listeria sp. were determined on brain-heart agar which contained 5% sheep erythrocytes. Minimal bactericidal concentrations were determined in Mueller-Hinton broth with an inoculum of 10⁶ CFU with 0.1 ml plated from clear tubes to sheep blood agar plates. The minimal bactericidal concentration was the concentration at which no growth was observed on the agar plates.

The overall activity of midecamycin is given in Table 1. It inhibited the majority of streptococci, staphylococci, and Haemophilus influenzae at concentrations of ≤3.1 μg/ml. Streptococcus pneumoniae was inhibited at concentrations of ≤0.2 μg/ml. Midecamycin also inhibited Campylobacter jejuni at 3.1 μg/ml. Bacteroides fragilis had a considerably higher MIC of 25 μg/ml, and all of the Enterobacteriaceae and Pseudomonas spp. were resistant, with MICs of >100 μg/ml. Midecamycin did not inhibit Enterobacteriaceae or Pseudomonas spp., even when the assays for the organisms shown were performed at pH 8. All five isolates of each of the following species had midecamycin MICs of >100 μg/ml: Acinetobacter anitratum, Citrobacter diversus, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Morganella morganii, Providencia stuartii, Pseudomonas aeruginosa, other Pseudomonas spp., Serratia marcescens, and Shigella sonnei.

Table 2 shows the comparative activities of midecamycin, erythromycin, and several other agents against Listeria spp. and staphylococci. Midecamycin was less active than erythromycin.
against all the species. Furthermore, staphylococci and *Streptococcus faecalis* resistant to erythromycin were not inhibited by midecamycin. Erythromycin usually was two- to fourfold more active against most, but not all, isolates of staphylococci, streptococci, *H. influenzae*, and *S. pneumoniae*.

MICs were only slightly affected by increasing the inoculum size from $10^3$, $10^5$, and $10^7$ CFU when testing either *Staphylococcus aureus* or *Streptococcus mitis*. For example, MICs of 0.1 and 0.8 $\mu$g/ml at $10^5$ CFU became 0.2 and either 0.8 or 1.6 $\mu$g/ml at $10^7$ CFU. However, the minimal bactericidal concentrations increased from 1.6 and 3.1 $\mu$g/ml at $10^5$ CFU to 100 and $>100$ $\mu$g/ml at $10^7$ CFU.

Although midecamycin has activity similar to erythromycin against most gram-positive bacteria, in general it was less active than erythromycin in vitro in this study. We also did not find that the drug would inhibit staphylococci, streptococci, or *Listeria* spp. resistant to erythromycin, as has been reported (1). However, midecamycin has proved to be as effective as erythromycin and more protective than josamycin in mouse protection studies in which *S. aureus* was the pathogen (1). Clearly, further studies of the efficacy of midecamycin in treating human infections would be of value.

**LITERATURE CITED**