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In Vitro Susceptibility Studies with Josamycin and Erythromycin

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The in vitro activity of josamycin and erythromycin against five bacterial species was compared. In general, erythromycin was slightly more active by weight than josamycin, although both agents had a similar range of activity.

Josamycin is a macrolide antibiotic produced by *Streptomyces narbonensis* var. *josamyceticus*. It is similar to erythromycin, but does not induce macrolide resistance in staphylococci and appears to have a lower incidence of gastrointestinal side effects (3; M. A. Sande, L. J. Strausbaugh, J. M. Gwaltney, Jr., and J. A. Dilworth, Prog. Abstr. Intersci. Conf. Antimicrob. Agents Chemother., 15th, Washington, D.C., Abstr. 16, 1975). In this study the in vitro susceptibilities of *Mycoplasma pneumoniae*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Staphylococcus aureus*, and *Haemophilus influenzae* to josamycin and erythromycin were compared. Since erythromycin is used infrequently in the therapy of anaerobic infections, the susceptibility of *Bacteroides fragilis* to josamycin was compared with susceptibility to clindamycin.

All strains of *M. pneumoniae* were isolated in 1974 at Paris Island, S.C., from Marine recruits with pneumonia. The other test strains were clinical isolates obtained from the microbiology laboratory of the University of Virginia Hospital.

The minimum inhibitory concentrations (MICs) of josamycin and erythromycin for *M. pneumoniae* were determined by a microtiter broth dilution method (W. G. Dodd, J. O. Hendley, and J. M. Gwaltney, submitted for publication).

A microdilution method (2) was also used for the other four aerobic organisms. Serial twofold dilutions of freshly prepared stock solutions of josamycin (supplied by Stine Laboratories of E. I. DuPont de Nemours and Co., Wilmington, Del.) and erythromycin (supplied by Abbott Laboratories, North Chicago, Ill.) were made in heart infusion broth (Difco), using a semiautomatic multimicrodiluter (Cooke Engineering Co., Alexandria, Va.) and microdilution plates (Linbro Chemical Co., IS-MRC-96, New Haven, Conn.). Each well was inoculated with 10^5 colony-forming units obtained from dilution of an overnight culture. One-half percent defibrinated sheep blood was added to wells containing *S. pneumoniae*, *S. pyogenes*, and *H. influenzae*. The MIC was defined as the lowest concentration inhibiting visible turbidity after 18 h of incubation at 35 C in 10% CO_2.

Since the growth of *H. influenzae* strains produced less turbidity, the MICs could not be established with certainty; therefore, minimum bactericidal concentrations were determined for these isolates by subculturing clear wells on chocolate agar after 48 h of incubation. The minimum bactericidal concentration was the lowest antibiotic concentration achieving sterility.

The MICs for *B. fragilis* were determined by a macrodilution method. Serial twofold dilutions of josamycin and clindamycin (Upjohn Co., Kalamazoo, Mich.) were made in prereduced brain heart infusion tubes (Scott Laboratories, Fiskeville, R.I.), which were then inoculated with 10^5 colony-forming units. The MICs were determined as above after 18 h of incubation at 35 C.

Erythromycin was more active than josamycin against all five species (Table 1 and Fig. 1); however, all strains with the exception of *H. influenzae* isolates were susceptible to concentrations of josamycin achieved in serum after oral therapy (2 μg/ml) (1). More than 90% of *M. pneumoniae* strains were inhibited by 0.015 μg of erythromycin and 0.03 μg of josamycin per ml. Ninety-eight percent of *S. pneumoniae* and *S. pyogenes* isolates were inhibited by 0.06 μg of erythromycin and 0.25 μg of josamycin per ml. Josamycin was least active against *S. aureus* and *H. influenzae*. Whereas all 25 strains of *S. aureus* were susceptible to 0.25 μg of erythromycin per ml, 2.0 μg of josamycin per ml was required to inhibit these

TABLE 1. *MICs of josamycin and erythromycin for six species*

Species	No. of strains tested	Josamycin		Erythromycin		Clindamycin	
		Median	Range	Median	Range	Median	Range
Mycoplasma pneumoniae	46	0.015	0.007–0.25	0.007	0.0015–0.06		
Streptococcus pneumoniae	24	0.06	0.007–0.25	0.015	0.007–0.03		
Streptococcus pyogenes	25	0.125	0.06–0.50	0.015	0.007–0.125		
Staphylococcus aureus	25	1.0	0.5–2.0	0.25	0.125–0.25		
Haemophilus influenzae	26	4.0[a]	0.50–8.0	2.0	0.25–2.0		
Bacteroides fragilis	12	0.50	0.125–>8			0.125	<0.03–>8

[a] Minimum bactericidal concentration in micrograms per milliliter for all *H. influenzae* values.

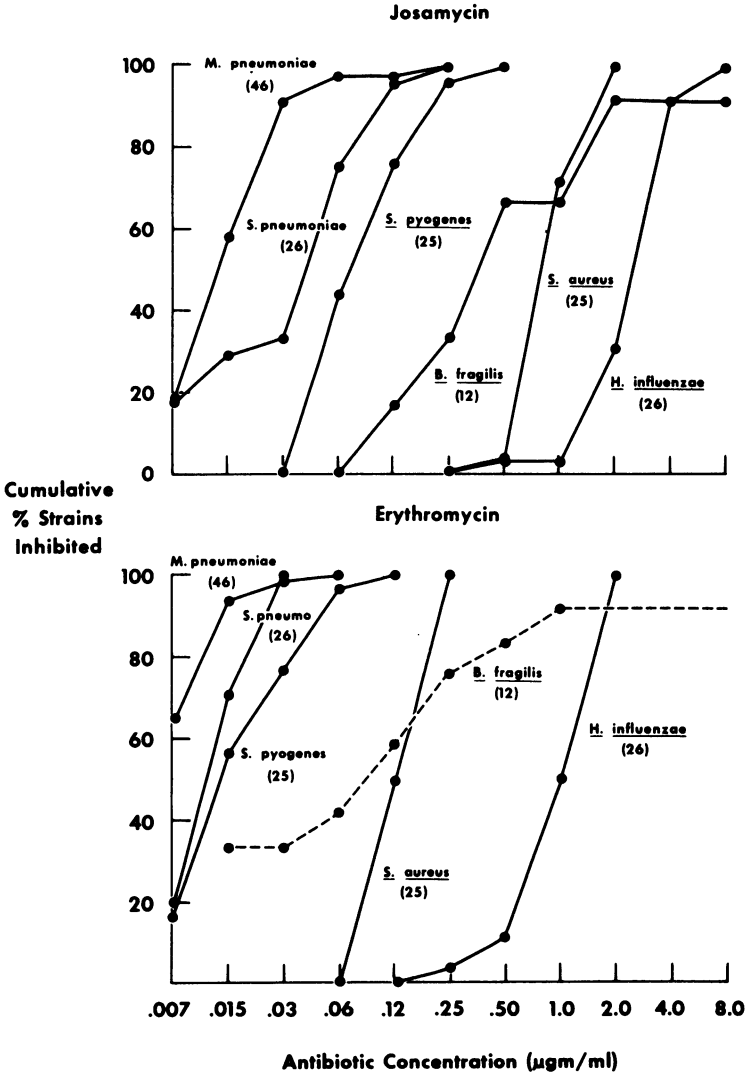

FIG. 1. *In vitro susceptibility of six species to josamycin and erythromycin. B. fragilis was tested against clindamycin (-----) instead of erythromycin. Number of strains tested indicated by number in parentheses.*

strains. Erythromyin at 2 μg/ml was bactericidal for the 26 strains of *H. influenzae*, but only 30% of the isolates were susceptible to this concentration of josamycin.

Clindamycin was more active than josamycin against *B. fragilis*, although 11 of the 12 strains were susceptible to 2.0 μg of josamycin per ml.

The results of this study agree with those of Japanese investigators (3). Josamycin and erythromycin have a similar spectrum of antibacterial activity, but josamycin is less active by weight against *M. pneumoniae*, *S. pyogenes*, *S. pneumoniae*, *S. aureus*, and *H. influenzae*. Josamycin is likewise less active than clindamycin against *B. fragilis*. With the exception of *H. influenzae* isolates, most strains were susceptible to concentrations of josamycin within the therapeutic range.

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