Susceptibility of Various Serogroups of Streptococci to Clindamycin and Lincomycin

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The minimal inhibitory concentration of lincomycin and clindamycin for a large number of strains from multiple serogroups of streptococci was determined. The median minimal inhibitory concentration for streptococci from groups A, B, C, F, G, H, L, and M and nongroupable organisms ranged from 0.02 to 0.39 μg of lincomycin per ml and from ≤ 0.01 to 0.09 μg of clindamycin per ml. Among the group D strains, *Streptococcus faecium* and *Streptococcus faecalis* were resistant to lincomycin and clindamycin, whereas *Streptococcus bovis* and four American strains of *Streptococcus durans* resembled nongroup D isolates in their susceptibility to these agents. Occasional strains of nongroup D streptococci were highly resistant to lincomycin and clindamycin.

Lincomycin and clindamycin (7 chloro-7 deoxylincomycin) are being used with increasing frequency to treat severe nonenterococcal streptococcal infections. The in vitro susceptibility to lincomycin and clindamycin of groups A, B, and D and nongroupable streptococci has been studied previously (4, 6-8, 12); however, there is little data regarding the susceptibility of other streptococci to these antibiotics. This study was undertaken to determine the susceptibility of the less common serogroups of streptococci to lincomycin and clindamycin and to examine in more detail the susceptibility patterns of the more frequently occurring groups of streptococci.

MATERIALS AND METHODS

Streptococci isolated from clinical specimens submitted to the Diagnostic Bacteriology Laboratory of the Massachusetts General Hospital were studied. In addition, reference strains of some of the less common serogroups obtained from the Center for Disease Control, Atlanta, Ga., and recent isolates from routine throat and stool specimens collected from natives of Ontong Java, British Solomon Islands Protectorate were also tested. The latter were included because they were recovered from an isolated atoll population who had never been exposed to lincomycin or clindamycin.

Strains were classified according to serological group by the Lancefield method using extracts obtained by the methods of Rantz and Randall (10) and Watson et al. (B. K. Watson, R. C. Moellering Jr., L. J. Kunz, and T. F. Medrek, Abst. Ann. Meet. Am. Soc. Microbiol. 1972, M200, p. 113). The group D streptococci were further speciated on the basis of

physiological and biochemical reactions using a composite of the reactions suggested by Deibel (1) and Facklam (3). These reactions which were used for speciation as well as their interpretation are detailed in a recent publication (9).

Agar plate dilution tests of in vitro antibiotic susceptibility were performed on Trypticase soy agar (BBL) with 5% defibrinated sheep blood. Agar plates, containing serial twofold dilutions of antibiotic at final concentrations ranging from 100 to 0.01 $\mu\text{g}/\text{ml}$, were inoculated using the inocula replicating technique of Steers et al. (11). This technique delivered an aliquot of 0.002 ml of a visibly turbid overnight growth of organisms in Todd-Hewitt broth; the inoculum was estimated to contain approximately 10^8 viable organisms (12). The plates were examined for bacterial growth after 18 to 20 h of incubation at 37 C. The lowest concentration of antibiotic at which no growth was visible was considered the minimal inhibitory concentration (MIC). Control plates containing no antibiotic were inoculated in a similar fashion with each series of susceptibility tests to assess strain viability. The reproducibility of the test was evaluated by including three reference strains of streptococci in each series of tests. The MIC of lincomycin and clindamycin for each of these three strains was consistently within one dilution of the originally observed MIC.

RESULTS

Among the streptococci studied, the median MIC of lincomycin for each serotype with the exception of the enterococci ranged from 0.02 to 0.39 $\mu\text{g}/\text{ml}$, whereas the comparable median MIC of clindamycin ranged from ≤ 0.01 to 0.09 $\mu\text{g}/\text{ml}$ (Table 1). In general, for each serotype examined, the median MIC of clindamycin was

TABLE 1. Susceptibility of selected streptococci to lincomycin and clindamycin^a

Serotype	No. of strains	MIC ^b (μg/ml)			
		Lincomycin		Clindamycin	
		Range	Median	Range	Median
Group A	25	≤0.01–0.09	0.02	≤0.01–0.04	≤0.01
Group B	25	0.04–0.19	0.09	0.02–0.09	0.04
Group C	25	0.09–1.5	0.19	≤0.01–0.78	0.04
Group D					
enterococci					
<i>S. faecium</i>	12	0.39–100	25	0.09–100	12.5
<i>S. faecalis</i>	21	6.2–100	25	0.78–100	25
<i>S. durans</i> ^c	4	0.09–3.1	0.19	0.04–0.78	0.09
nonenterococci					
<i>S. bovis</i>	22	0.04–0.39	0.09	≤0.01–0.09	≤0.01
Group F	27	0.09–12.5	0.39	≤0.01–0.09	0.04
Group G	25	0.04–0.19	0.09	0.02–0.09	0.04
Group H	17	0.09–100	0.39	0.02–50	0.04
Group L	15	≤0.01–0.39	0.19	≤0.01–0.09	0.04
Group M	12	0.02–50	0.19	0.02–6.2	0.04
Nongroupable	35	0.02–50	0.19	≤0.01–50	0.04

^a Isolates from clinical specimens submitted to Massachusetts General Hospital Bacteriology Laboratory.^b Inocula replicating method.^c Three reference strains, one clinical isolate.

2 to 10 times less than that of lincomycin. The relative lincomycin and clindamycin susceptibility of strains from the serotypes studied are shown in Fig. 1–3. Streptococci from groups A, B, and G and *Streptococcus bovis* were the most susceptible to lincomycin, whereas those from groups A, B, G, F, and L and *S. bovis* were exquisitely susceptible to clindamycin. Of the streptococci studied, the vast majority from all serotypes were inhibited by concentrations of ≤0.5 μg/ml of lincomycin or clindamycin. The major exception to this susceptibility pattern was the enterococcal group D strains, where MIC values of ≥3.1 μg/ml of lincomycin and clindamycin were frequent. Strains of streptococci within most serotypes demonstrated a fairly narrow range of MIC values for these antibiotics. However, this did not prove to be true for the group D streptococci. The nonenterococcal group D streptococci, including *S. bovis*, as well as the enterococcal *Streptococcus durans* strains, were strikingly more susceptible to lincomycin and clindamycin than the other enterococcal group D isolates, *Streptococcus faecium* and *Streptococcus faecalis*. The antibiotic susceptibility pattern of the *S. durans* strains isolated in the Solomon Islands resembled that of “American” enterococci, particularly *S. faecium*. Occasional strains of groups F, H, M, O, P, and Q and some nongroupable streptococci were less susceptible to lincomycin and clindamycin than other similarly sero-

FIG. 1. Susceptibility of various common serogroups and nongroupable streptococci to clindamycin (upper panel) and lincomycin (lower panel). Abbreviations: A, B, C, D, F, G, H = serogroup. NGr = nongroupable. Numbers in parentheses represent number of strains tested.

FIG. 2. Susceptibility of various less common serogroups of streptococci to clindamycin (upper panel) and lincomycin (lower panel). Abbreviations: E, K, L, M, N, O, P, Q, R, S, T, U = serogroup. Numbers in parentheses represent number of strains tested.

grouped strains. The MIC of lincomycin and clindamycin for these more resistant strains ranged from 3.1 to 100 $\mu\text{g/ml}$.

In general, the *in vitro* susceptibility to lincomycin and clindamycin of strains of streptococci isolated from natives of the Solomon Islands paralleled closely the susceptibility pattern of the respective species of streptococci isolated at the Massachusetts General Hospital (Fig. 1-3).

DISCUSSION

Streptococci belonging to serogroup A (4, 6-8), B (7), and nongroupable strains (4, 6-8) have been previously shown to be susceptible *in vitro* to lincomycin and clindamycin. This study confirms these results. In addition, the low MIC of lincomycin and clindamycin for streptococci in serogroups C, F, G, H, L, and M indicates that streptococci in these groups are also highly susceptible to both antibiotics. With the major exception of the group D streptococci

the range of MIC values for lincomycin and clindamycin against organisms in a given serogroup was narrow. Occasionally, however, strains of streptococci from groups F, H, M, O, P, and Q and nongroupable isolates were significantly more resistant than other serologically similar strains.

Previous studies have suggested that the group D streptococci are resistant to clindamycin and lincomycin (4, 6-8, 12). With the exception of Toala et al. (12), whose studies were limited to enterococci, none of the previous investigators have speciated the group D streptococci. This is important because the group D streptococci consist of so-called enterococci (especially *S. durans*, *S. faecalis*, and *S. faecium*) as well as nonenterococcal strains, the most important of which are *S. bovis* (9). When the group D streptococci are carefully speciated, it is clear that not all group D streptococci are resistant to clindamycin and lincomycin. Virtually all strains of *S. faecalis* and *S. faecium*, which are enterococci, proved resistant to clinically achievable levels of lincomycin and clindamycin as has been shown in previous studies. However, the four "American" strains of *S. durans* (which are also enterococci), as well as the strains of *S. bovis*, were quite susceptible to

FIG. 3. Susceptibility of various species of group D streptococci to clindamycin (upper panel) and lincomycin (lower panel). Numbers in parentheses represent number of strains tested.

both antibiotics. Three of the four American strains of *S. durans* were reference strains which had been maintained in the laboratory for an extended period and thus possibly altered. Nevertheless, the divergent susceptibility patterns of the American *S. durans* and *S. bovis* strains as contrasted with *S. faecalis* and *S. faecium* may have important clinical implications and re-emphasizes the importance of careful speciation of the group D streptococci.

Interestingly, the *S. durans* strains isolated in the Solomon Islands demonstrated a susceptibility pattern similar to the "American" strains of *S. faecium*. This is not surprising since these organisms are closely related and are, in fact, distinguished only by their ability to ferment certain sugars, the most important of which are mannitol and arabinose. The Solomon Islands strains of *S. durans* failed to ferment mannitol, but were variable in their ability to ferment arabinose. Moreover, all produced acid from sucrose, a characteristic in common with *S. faecium*. Thus, it is quite possible that these strains are more closely related to *S. faecium* (or are biochemical variants of *S. faecium*) than the "American" strains of *S. durans* (all of which failed to ferment mannitol, arabinose, and sucrose). With the above noted exception, there was no significant difference in susceptibility of the Solomon Islands streptococci, which had not been previously exposed to lincomycin or clindamycin, when compared with similar serogroups isolated in America.

Our studies point out the importance of careful identification and speciation of streptococci when considering the clinical use of lincomycin or clindamycin for streptococcal infections. Previous investigators have reported that lincomycin and clindamycin are effective agents for the treatment of serious infection caused by nongroup D streptococci (5, D. A. Ronig, F. Cox, D. Pohlod, and E. L. Quinn. Prog. Abstr. Intersci. Conf. Antimicrob. Agents Chemother., 11th, Atlantic City, N.J., Abstr. 99, p. 50). Dixon and Lipinski (2), moreover, found only 0.05% of 18,628 group A streptococci resistant to lincomycin. Our findings support these observations, although the occurrence of an occasional highly resistant isolate among certain serogroups other than group D indicates the need for individual susceptibility testing when severe infections due to groups F, H, M,

O, P, Q, or the nongroupable streptococci are to be treated with lincomycin or clindamycin. While the enterococci are generally resistant to clindamycin and lincomycin, our studies suggest that the nonenterococcal group D streptococci and possible *S. durans* may be susceptible to lincomycin and clindamycin. This further emphasizes the importance of speciation and individual antibiotic susceptibility testing when major infections due to group D streptococci are encountered.

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