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Activity of Nine Antimicrobial Agents Against Lancefield Group C and Group G Streptococci

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The activity of nine antimicrobial agents against 44 strains of group C and group G streptococci was studied using a microtiter broth dilution technique. Several antimicrobial agents, including third-generation cephalosporins, the newer semisynthetic penicillins, and erythromycin, exhibited good activity against the organisms. Occasional tolerance to various agents was observed. No cross-tolerance was observed in this study.

Lancefield group C and group G streptococci, though uncommon pathogens, have been reported to cause a variety of serious infections (7, 8, 13, 15–17). These organisms are usually susceptible to penicillin (3, 4), but poor responses to penicillin therapy have been described in serious infections (endocarditis and septic arthritis) (2, 5). Tolerance to penicillin G, cephalothin, and vancomycin has been reported (9, 10). Though the clinical significance of tolerance is not clear, experimental and clinical evidence indicates that it may adversely affect the response to therapy of endocarditis (11, 12).

We tested 44 strains (25 group C and 19 group G) in this study. All strains were human isolates and were identified serologically by the Phadebact coagglutination reaction (6). Two control strains (*Staphylococcus aureus* ATCC 25923 and *Streptococcus faecalis* ATCC 33186) were used with each susceptibility testing run.

Antimicrobial solutions were prepared in distilled water from laboratory standard powders kindly provided as follows: erythromycin from Bristol Laboratories, Syracuse, N.Y.; azlocillin from Delbay Research Corp, West Haven, Conn.; penicillin G, vancomycin, moxalactam, and cephalothin from Eli Lilly & Co., Indianapolis, Ind.; cefmenoxime from Abbott Laboratories, North Chicago, Ill.; cefotaxime from Hoechst-Roussel Pharmaceuticals Inc., Somerville, N.J.; and piperacillin from Lederle Laboratories, Pearl River, N.Y. They were dispensed into microtiter plates and diluted using the Dynatech MIC-2000 (Dynatech Laboratories, Inc., Alexandria, Va.).

Minimal inhibitory concentrations (MICs) were determined by a microtiter broth dilution technique similar to the one described by Barry et al. (1). A standard bacterial suspension was prepared in Todd-Hewitt broth to an inoculum of 10^8 colony-forming units per ml (adjusted to correspond to a 0.5 Macfarland standard). A 1-ml amount of this inoculum was diluted in 9 ml of distilled water. The microtiter plates were inoculated with 0.001 ml of inoculum in each well containing 100 μl of antimicrobial solution to give a final inoculum of 10^5 colony-forming units per ml. The microtiter plates were then incubated for 24 h at 35°C in room air. The MIC of each antimicrobial agent was read as the lowest concentration that prevented growth in the wells.

Minimal bactericidal concentration (MBC) was determined by inoculating 0.01 ml of suspension from each well of the microtiter plate onto Mueller-Hinton agar with 15% sheep blood and incubating for 24 h. The MBC was read as the lowest concentration of the antimicrobial agent at which no growth occurred. This method will detect 99.9% death in the original inoculum.

Table 1 summarizes the results of this study. Reproducible results were obtained with both control strains, with MICs and MBCs ranging within one dilution of the mean. Most strains of group C and group G streptococci were susceptible to all of the antimicrobial agents tested. Two strains demonstrated tolerance (defined as an MIC/MBC ratio of 32 or greater) to penicillin G, and one strain demonstrated tolerance to vancomycin, one to cephalothin, one to piperacillin, and one to moxalactam (Table 2). The newer semisynthetic penicillins and the third-generation cephalosporins, except moxalactam, exhibited excellent activity against both organisms, with MICs and MBCs ranging from 0.03 to 1 μg/ml. Good activity was also observed with erythromycin.

The organisms exhibited moderate susceptibility to maxolactam, with the 90% MIC being 8 μg/ml. This is similar to the susceptibility of

TABLE 1. MIC and MBC ranges of nine antimicrobial agents against 44 isolates of group C and group G streptococci

Drug	MIC (μg/ml)			MBC range (μg/ml)
	Range	50%	90%	
Penicillin	0.03–0.06	0.03	0.03	0.03–32
Vancomycin	0.03–0.5	0.06	0.12	0.03–4
Cephalothin	0.03–0.5	0.03	0.06	0.03–1
Cefmenoxime	0.03–0.12	0.03	0.06	0.03–0.12
Cefotaxime	0.03–0.25	0.03	0.12	0.03–0.25
Moxalactam	0.03–8.0	2.0	8.0	0.03–8.0
Piperacillin	0.03–0.5	0.03	0.03	0.03–0.5
Azlocillin	0.03–0.25	0.03	0.06	0.03–0.25
Erythromycin	0.03–1.0	0.12	1.0	0.03–4.0

TABLE 2. MIC and MBC of five antimicrobial agents against tolerant group C and group G streptococci[a]

Streptococcal group	Penicillin G		Cephalothin		Vancomycin		Piperacillin		Moxalactam	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
C	**0.03**	**32.0**	0.03	0.03	0.5	0.5	0.12	0.12	0.5	0.5
C	**0.03**	**32.0**	0.03	0.03	0.12	0.12	0.03	0.03	0.5	0.5
C	0.03	0.03	**0.03**	**1.00**	0.25	0.25	0.03	0.03	2.0	2.0
G	0.03	0.03	0.03	0.03	**0.12**	**4.0**	0.03	0.03	1.0	1.0
G	0.03	0.03	0.03	0.12	0.5	0.5	**0.03**	**0.5**	8.0	8.0
G	0.03	0.03	0.03	0.03	0.12	0.12	0.03	0.03	**0.03**	**1.0**

[a] MICs and MBCs are given in micrograms per milliliter. Numbers in boldface indicate tolerance of the strain to the drug.

group B streptococci which require between 8 and 16 μg/ml for inhibition. Since moxalactam is currently not recommended for group B infections (14), particularly those of the central nervous system, it would seem prudent to extend the same reservation to group C and group G streptococcal infections.

Penicillin retains its place as the drug of choice in infections due to group C and group G streptococci. Tolerance, however, has been demonstrated and may on occasion account for the slow response seen in serious infections. We did not observe cross-tolerance, and several alternatives to penicillin are available, including newer semisynthetic penicillins and third-generation cephalosporins. In patients allergic to penicillin, vancomycin and erythromycin are adequate substitutes, but careful testing of inhibitory and bactericidal activity may still be necessary.

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