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Comparative In Vitro Activities of Teichomycin and Other Antibiotics Against JK Diphtheroids

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The in vitro susceptibilities of 98 isolates of JK diphtheroids to teichomycin, vancomycin, and eight other antibiotics was investigated. Teichomycin and vancomycin were extremely active against all the isolates tested. The 90% minimal inhibitory concentrations for teichomycin and vancomycin were 1.56 and 0.78 μg/ml, respectively. The majority of the isolates were resistant to ticarcillin, methicillin, erythromycin, tetracycline, chloramphenicol, clindamycin, and cephalothin.

Sepsis caused by a *Corynebacterium* species that was resistant to multiple antibiotics was first reported in 1976 and 1977 (3, 4, 8). This group of diphtheroids has been designated group JK by the Special Bacteriology Section, Centers for Disease Control, Atlanta, Ga., and was first well characterized in 1979 by Riley et al. (9). Since then, the organism has been reported to be a cause of prosthetic valve endocarditis, ventriculo-atrial shunt infection and shunt nephritis, nonprosthetic valve endocarditis, empyema-,brain abscess, and other serious infections (2, 6, 10). JK diphtheroids are being cultured with increasing frequency from patients with cancer, especially those with hematological malignancies. These organisms are uniformly and predictably susceptible only to vancomycin in vitro and infrequently to rifampin and tetracycline. Teichomycin is a new antibiotic with a chemical structure similar to that of vancomycin, which has good activity in vitro against most gram-positive organisms (V. Fainstein, S. Weaver, and G. P. Bodey, Program Abstr. Intersci. Conf. Antimicrob. Agents Chemother. 22nd, Miami, Fla., abstr. no. 617, 1982). We have investigated the activity of teichomycin against isolates of JK diphtheroids cultured from cancer patients and compared it with those of other available antibiotics.

MATERIALS AND METHODS

Bacterial strains. A total of 98 strains of JK diphtheroids were studied. Of these, 77 were cultured from blood specimens obtained from cancer patients at The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston from 1976 through 1981. The remaining strains were cultured from specimens of skin, nose, throat, or other miscellaneous sites. All isolates were maintained in stock by ultrafreezing methods. The organisms were identified as belonging to the group JK by criteria outlined in a previous report (9). The organisms were catalase positive, oxidase negative, and did not reduce nitrate or hydrolyze urea. All strains acidified glucose but not sucrose; 90% of the strains acidified maltose and at 24 and 48 h produced no change on the triple sugar iron agar slant. In contrast, both *Corynebacterium diphtheriae* and *Corynebacterium minutissium* produce alkaline or acid reactions on the slant after the same incubation period. All strains that were maltose negative were also negative for *o*-nitrophenyl-β-D-galactopyranoside, ruling out *Corynebacterium bovis*. All fermentation reactions were held for 3 weeks (1).

Organisms were inoculated in brain heart infusion with 5% rabbit serum and incubated at 37°C in a CO_2 incubator for 24 h (6). Appropriate dilutions were made so that the concentration in the inocula was 10^7 organisms per ml (5).

Antimicrobial agents. The antimicrobial agents studied were: teichomycin (Dow Chemical Co., Indianapolis, Ind.), vancomycin, cephalothin, rifampin, methicillin, ticarcillin, erythromycin, tetracycline, chloramphenicol, and clindamycin. All solutions were prepared manually in brain heart infusion with 5% rabbit serum and serially diluted twofold from 1,000 μg/ml. They were then dispensed automatically by an MIC 2000 dispenser (Dynatech Laboratories, Inc., Alexandria, Va.).

Susceptibility tests. All isolates were tested in brain heart infusion with 5% rabbit serum. All of the plates were inoculated automatically with a volume of 0.0015 ml of the suspension of organisms (10^7 organisms per ml) into 0.10 ml of the appropriate antibiotic concentration per well, giving a final concentration of 1.5×10^5 organisms per ml. The plates were then incubated at 37°C in a CO_2 incubator for 48 h. Readings were taken at 24 and 48 h. *Escherichia coli* and *Pseudomonas aeruginosa* isolates were used as controls.

Definitions. The minimal inhibitory concentration (MIC) was defined as the lowest concentration of drug that suppressed visible growth after incubation at 37°C in a CO_2 incubator for 24 h. There was no difference in the readings at 24 and 48 h. The minimal bactericidal concentration (MBC) was defined as the lowest con-

centration of drug that yielded fewer than five colonies on subculture in sheep blood agar (≥99% killing) after incubation at 37°C in a CO_2 incubator for 24 h. A micropipetting device was used to deliver 10 μl of solution for subculture. All strains were also tested for β-lactamase production by a chromogenic cephalosporin method (6, 7).

RESULTS

The results of the in vitro susceptibility tests are shown in Table 1. The most effective agents were vancomycin, teichomycin, and rifampin. At a concentration of 0.78 μg of vancomycin per ml, 90% of the isolates were inhibited. Teichomycin inhibited 96% of isolates at a concentration of 1.56 μg/ml. MBCs for both vancomycin and teichomycin were one to two dilutions higher than MICs for the majority of isolates. The MBC of vancomycin for three isolates was fourfold higher than the MIC. Rifampin inhibited 99% of the isolates at a concentration of 0.10 μg/ml; however, the rifampin MBC was 2- to 10-fold higher than the MIC for 60% of the isolates.

Tetracycline and chloramphenicol showed MICs in the intermediate to high range (1.56 to >100 μg/ml). The percentage of isolates inhibited by tetracycline at a concentration of 25 μg/ml and by chloramphenicol at a concentration of 50 μg/ml was 50%; the corresponding MBCs showed a high level of resistance, the majority being ≥100 μg/ml.

As noted in previous studies, JK diphtheroids were highly resistant to methicillin, ticarcillin, cephalothin, clindamycin, and erythromycin. MICs were >100 μg/ml for more than 90% of the isolates. Even among the more susceptible isolates, the MBCs were >100 μg/ml. None of the isolates produced β-lactamases when tested with a chromogenic cephalosporin.

TABLE 1. In vitro susceptibility of 98 isolates of group JK bacteria

Drug	MIC (μg/ml)[a]		
	50%	90%	Range
Vancomycin	0.78	0.78	≤0.20–≤6.25
Teichomycin	0.78	1.56	≤0.10–≤25
Rifampin	0.05	0.05	≤0.05–≥50
Methicillin	>100	>100	≤0.20–≥100
Ticarcillin	>100	>100	≤0.39–≥100
Cephalothin	>100	>100	≤0.10–≥100
Erythromycin	>100	>100	≤0.20–≥100
Tetracycline	25	100	≤1.56–≥100
Chloramphenicol	50	50	≤3.12–≥100
Clindamycin	>100	>100	≤0.10–≥100

[a] 50% and 90%, MICs that inhibited 50 and 90% of the strains, respectively.

DISCUSSION

Teichomycin is a new antibiotic that has been known to be effective against the majority of gram-positive organisms, including resistant *Staphylococcus epidermidis*, *Staphylococcus aureus*, and *Enterococcus* spp. (22nd ICAAC, abstr. no. 617). Its expanded spectrum of activity resembles that of vancomycin. We have shown that it is as effective as vancomycin in vitro against this group of bacteria and therefore deserves clinical evaluation.

JK diphtheroids were extremely susceptible to rifampin, as previously reported, although much higher concentrations were required for bactericidal activity. The wide range of corresponding rifampin MBCs is of concern because bactericidal activity may be preferable to treat infections in patients with neutropenia.

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