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Antimicrobial Susceptibility of *Corynebacterium* Group D2

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The in vitro susceptibility of 30 *Corynebacterium* group D2 strains to nine antimicrobial agents was determined. Vancomycin and norfloxacin were the most active agents tested. All strains were resistant to ampicillin and cephalothin, all except one were resistant to gentamicin, and the activity of erythromycin, novobiocin, tetracycline, and rifampin varied.

Corynebacterium group D2 is a microorganism described by King (4) as a gram-positive bacillus whose culture and biochemical characteristics resemble those of *Corynebacterium* group JK (5). The urease activity and the inability to acidify glucose are the main differences between group D2 and the better-known group JK. *Corynebacterium* group D2 was isolated from the transtracheal aspirates of an elderly patient with pneumonia (2) and was recently involved in alkaline-encrusted cystitis (6), a very severe urinary tract infection which is difficult to treat. The urease activity of this microorganism seems to play an important role in its pathogenicity, which is usually associated with alkaline urine (pH higher than 8.0) and struvite (ammonium magnesium phosphate) stones. These two conditions surely contribute to its pathogenicity and create unfavorable environmental conditions for the efficient action of most antimicrobial agents.

Only a few strains of *Corynebacterium* group D2 have been tested against some antimicrobial agents (3, 6), indicating that it could be of interest to test more clinical isolates against other drugs to define its susceptibility profile, taking into account the effect of alkalinity on the activity of the antimicrobial agents.

Thirty strains of *Corynebacterium* group D2 isolated from different patients were studied. Twenty-nine isolates were from urine samples, and one was from perirenal drainage. Antimicrobial susceptibilities were studied by the agar dilution method to determine the MICs of nine drugs. The inoculum was prepared from a 24-h culture in Mueller-Hinton broth (Difco Laboratories) containing 25% sterile rabbit serum and 1% Tween 80 and adjusted to the turbidity of a 0.5 McFarland standard. A 1:10 dilution of the standardized tubes was made in tryptic soy broth (Difco) and inoculated with a Steers replicator onto two sets of Mueller-Hinton agar (Difco) (pH 7.4 and 8.5) containing twofold increasing concentrations of antimicrobial agents. The drugs tested were ampicillin (Beecham Laboratories), cephalothin (Eli Lilly & Co.), erythromycin (Abbott Laboratories), rifampin (Lepetit), tetracycline (Pfizer Inc.), vancomycin (Dista), novobiocin (Merck Sharp & Dhome), norfloxacin (Liade), and gentamicin (Schering Corp.). The plates were incubated for 24 h at 37°C and examined for growth. The MIC was defined as the lowest concentration of antimicrobial agent at which the isolate failed to grow.

Table 1 shows the MICs of the nine antimicrobial agents tested against the 30 strains of *Corynebacterium* group D2 with media at two pHs (7.4 and 8.5). All strains were susceptible to vancomycin and norfloxacin and resistant to ampicillin and cephalothin. The activity of all the other five drugs varied. Of the 30 strains studied, 27 were susceptible to novobiocin (MIC, ≤8 μg/ml), 29 were susceptible to rifampin (MIC, ≤8 μg/ml), and only 1 was susceptible to gentamicin (MIC, ≤0.25 μg/ml); the MICs for all the others were ≥1,024 μg/ml. A bimodal response to erythromycin was observed; the MICs were ≤0.25 μg/ml for 5 strains, ≥1,024 μg/ml for 23 strains, and in the middle range (64 and 128 μg/ml) for only 2 strains. Tetracycline was moderately active against these microorganisms; the MICs were ≤2 μg/ml for 4 strains, 4 to 16 μg/ml for 20 strains, 32 to 64 μg/ml for 6 strains. There was no evident relationship between the susceptibility or resistance data for these microorganisms and one or more drugs.

The isolation of *Corynebacterium* group D2 is exceptional

TABLE 1. Susceptibility of 30 strains of *Corynebacterium* group D2 to nine antimicrobial agents

Drug	MIC (μg/ml) at indicated pH					
	7.4			8.5		
	Range	50%[a]	90%[b]	Range	50%[a]	90%[b]
Erythromycin	0.06–>1,024	1,024	>1,024	0.03–1,024	1,024	1,024
Norfloxacin	0.5–4	1	2	0.5–8	2	4
Novobiocin	≤0.25–32	0.5	8	4–>1,024	8	128
Vancomycin	≤0.25–0.5	0.5	0.5	1–8	4	8
Tetracycline	≤0.25–64	8	32	0.5–128	64	128
Rifampin	≤0.25–512	4	8	≤0.25–>1,024	128	>1,024
Cephalothin	128–1,024	256	1,024	256–>1,024	512	>1,024
Ampicillin	256–>1,024	>1,024	>1,024	512–>1,024	>1,024	>1,024
Gentamicin	≤0.25–>1,024	>1,024	>1,024	≤0.25–>1,024	>1,024	>1,024

[a] MIC for 50% of the strains.
[b] MIC for 90% of the strains.

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in many clinical laboratories but, when adequate microbiological techniques are used, its isolation from clinical specimens, mainly urine samples, may be higher than previously reported. This bacterium has been involved in alkaline-encrusted cystitis (6), a severe infection which is very difficult to treat, and perhaps in other clinical conditions (2), as is the case with other gram-positive bacilli, especially in immunosuppressed hosts (7). For all these reasons, knowledge of its antimicrobial susceptibility could be useful in the initial treatment of serious infections caused by it. Vancomycin and norfloxacin were uniformly active against *Corynebacterium* group D2, such that norfloxacin could be used in urinary tract infections and vancomycin could be reserved for more serious and generalized infections. Novobiocin, tetracycline, and rifampin could also be useful for the treatment of urinary tract infections because the concentrations of these drugs in urine were well above the MICs for most of the strains tested (1). A few strains were highly susceptible to erythromycin, and this drug, as well as novobiocin, tetracycline, and rifampin, could be of some use singly or in combination.

Most of the antimicrobial agents tested were less active at a high pH, which could be a disadvantage, owing to the fact that most of the urinary tract infections produced by this microorganism are associated with alkaline urine, probably in relation to the strong urease activity of *Corynebacterium* group D2. This urease activity can be inhibited by acetohydroxamic acid (6) such that its association with some active antimicrobial agents could be beneficial.

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