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In Vitro Activities of Antimicrobial Agents against Clinical Isolates of *Flavimonas oryzihabitans* Obtained from Patients with Cancer

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We evaluated the in vitro activities of 21 different antimicrobial agents against nine clinical isolates of *Flavimonas oryzihabitans* obtained from patients with cancer. The organisms were susceptible to most agents commonly used for the empiric therapy (aminoglycosides, ureidopenicillins, extended-spectrum cephalosporins, monobactams, and carbapenems) and prevention of infections (quinolones and trimethoprim-sulfamethoxazole) in this patient population.

Bacteria of the CDC Ve group were first described by Tatum et al. in 1974 and were subdivided into Ve-1 and Ve-2 biotypes on the basis of flagellar morphology, biochemical reactions, and DNA composition (16). They are aerobic, mobile, yellow-pigmented, catalase-positive, gram-negative rods with a cellular fatty acid composition similar to that of *Pseudomonas* species (5, 8). However, unlike *Pseudomonas* species, the Ve strains are oxidase negative. Recently, group Ve-1 has been designated *Chryseomonas luteola* and group Ve-2 has been designated *Flavimonas oryzihabitans* (7). These species differ from each other with regard to several biochemical reactions and the guanine-plus-cytosine content of their DNA (5). Their flagellar morphologies are also different, with *C. luteola* possessing multitrichous polar flagella and *F. oryzihabitans* possessing a single polar flagellum (16). Both organisms produce smooth, round colonies at 24 h, with various degrees of yellow pigmentation (5, 8). After 48 h, the colonies may appear more rough or wrinkled, particularly in the case of *F. oryzihabitans*.

The most common infections due to these organisms include bacteremia, wound infections, prosthetic valve endocarditis, peritonitis in patients undergoing continuous ambulatory peritoneal dialysis, and meningitis in patients following neurosurgery (1–3, 6, 9–11, 13, 14). A survey of the microbiological records of our institution revealed no documented infections due to *F. oryzihabitans* between 1980 and 1989 but 13 cases of infection between 1989 and 1992. Nine of these isolates were available for susceptibility testing. We tested the in vitro activities of 21 agents commonly used at our institution for the prevention (prophylaxis) of or empiric therapy of febrile episodes in cancer patients against these nine isolates of *F. oryzihabitans*. Our results form the basis of this report.

All organisms were isolated from blood culture specimens obtained from cancer patients who were treated at the University of Texas M. D. Anderson Cancer Center at Houston between 1989 and 1992. These organisms were stored in our laboratory by ultrafreezing methods. To avoid duplication of strains, only one isolate per patient was used from patients with multiple positive blood cultures. All antimicrobial agents were obtained from their respective manufacturers in the form of standard powders of known potency for laboratory use. These powders were kept frozen at −70°C until use. In vitro susceptibility determinations were carried out by a previously described microtiter broth dilution method in accordance with guidelines established by the National Committee for Clinical Laboratory Standards (12, 15). Briefly, the organisms were inoculated into broth and incubated overnight at 37°C. Appropriate dilutions were made so that the final inoculum tested was 5×10^5 CFU/ml. The test medium was cation-adjusted Mueller-Hinton broth (Difco Laboratories, Detroit, Mich.). The antibiotic concentrations tested ranged between 64.0 and 0.03 μg/ml. *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 were used as control strains to ensure the validity of the results. The MIC was defined as the lowest concentration of each drug that inhibited visible growth after incubation at 35°C for 16 to 20 h.

Since fewer than 10 organisms were available for testing, MIC ranges rather than the MICs for 50% and 90% of the strains are shown in Table 1. The microorganisms were uniformly susceptible to the aminoglycosides (amikacin, tobramycin, and gentamicin), with MICs ranging from 0.06 to 2.0 μg/ml. All three ureidopenicillins (azlocillin, mezlocillin, and piperacillin) were active against these isolates, with MICs ranging from 1.0 to 8.0 μg/ml. The combination of ticarcillin and clavulanic acid was also active against *F. oryzihabitans*. The ureidopenicillins were far more active against *F. oryzihabitans* than ampicillin and ampicillin-sulbactam (MIC range, 8.0 to 32.0 μg/ml each). All five broad-spectrum cephalosporins tested had similar activities against these isolates, with all five inhibiting 100% at a concentration of 2.0 to 4.0 μg/ml. The carbapenem imipenem was more active (MIC range, 0.12 to 1.0 μg/ml) against these isolates than the monobactam aztreonam, although all nine isolates were susceptible to aztreonam (MIC range, 0.5 to 8.0 μg/ml). Among the newer quinolones ciprofloxacin had the best activity against *F. oryzihabitans*, with all isolates being susceptible to a concentration of 0.06 μg/ml. Ofloxacin, fleroxacin, and temafloxacin were also quite active, although one isolate needed 4.0 μg of fleroxacin per ml for inhibition. All nine isolates were also quite susceptible to the combination of trimethoprim and sulfamethoxazole (TMP-SMX) (MIC range, 0.4-7.6 to 0.8-15.0 μg/ml).

Very few data regarding the susceptibility of *F. oryzihab-*

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TABLE 1. In vitro activities of 21 antimicrobial agents against nine clinical isolates of *F. oryzihabitans*

Antimicrobial agent	MIC range (μg/ml)
Amikacin	0.25–1.0
Tobramycin	0.06–2.0
Gentamicin	0.12–1.0
Ampicillin	8.0–32.0
Ampicillin-sulbactam	4.0–32.0
Azlocillin	1.0–4.0
Mezlocillin	1.0–8.0
Piperacillin	1.0–4.0
Ticarcillin-clavulanate	2.0–8.0
Ceftriaxone	0.25–4.0
Cefoperazone	0.25–4.0
Ceftazidime	0.12–2.0
Cefotaxime	0.25–4.0
Cefpirome	0.12–2.0
Aztreonam	0.5–8.0
Imipenem	0.12–1.0
Ciprofloxacin	0.03–0.06
Ofloxacin	0.06–1.0
Fleroxacin	0.5–4.0
Temafloxacin	0.25–1.0
TMP-SMX	0.4-76–0.8-15.0

itans have been reported to date because of the rarity of these organisms being isolated from clinical specimens. Data gleaned from previous case reports in the literature indicate that these organisms are generally resistant to narrow- and extended-spectrum cephalosporins but susceptible to broad-spectrum cephalosporins (3, 4, 6, 9, 13, 14). They are also usually susceptible to ampicillin, the carboxy- and ureidopenicillins, the aminoglycosides, the quinolones, TMP-SMX, the tetracyclines, and chloramphenicol. However, isolates resistant to ampicillin, chloramphenicol, ticarcillin, cefotaxime, aztreonam, and TMP-SMX have been reported (11, 13).

Patients with cancer are susceptible to infection by opportunistic pathogens that seldom cause disease in the immunocompetent host. The pressure of heavy antimicrobial agent usage in neutropenic cancer patients for infection prevention and for therapy can lead to the emergence of resistant organisms in such patients. Although we have seen an increase in the number of infections caused by *F. oryzihabitans* at our institution during the past 3 to 4 years, our data indicate that these organisms are quite susceptible to most of the agents used for infection prevention (TMP-SMX and quinolones) or empiric therapy (extended-spectrum cephalosporins, monobactams, carbapenems, ureidopenicillins, and aminoglycosides) of infections in neutropenic cancer patients. Imipenem and ciprofloxacin appear to be consistently active against these isolates and could be considered agents of choice for the treatment of infections caused by *F. oryzihabitans*.

Currently available data are insufficient to get a complete picture of the susceptibility of *F. oryzihabitans* to various antimicrobial agents. Although our report adds to the fund of current knowledge, various centers need to continue monitoring and reporting of the susceptibility of these organisms, as more of them are isolated from clinical specimens, to complete the picture.

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