Effect of Aztreonam on Throat and Stool Flora of Cancer Patients

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Eighteen patients with hematological malignancies received aztreonam in one of two dosing regimens, 1 or 2 g every 8 h for a total of 7 to 9 days. Throat and stool cultures were obtained before and during treatment with aztreonam. Aztreonam had little effect on the predominant throat flora. In contrast, facultatively anaerobic gram-negative bacilli were markedly decreased in stools during the administration of aztreonam. Strict anaerobes in the stool were variably affected by aztreonam.

Broad-spectrum antibiotics cause marked changes in gastrointestinal microbial flora (2). These changes are of particular interest in patients with hematological malignancies, since gut bacteria are often the cause of serious infection in these patients (3, 6). Aztreonam (SQ 26,776, formerly azthreonam) is a synthetic monobactam antibiotic with broad in vitro activity against aerobic (or facultatively anaerobic) gram-negative bacilli (7). Strict anaerobes often demonstrate resistance to the drug. This study evaluated serial throat and stool cultures in cancer patients receiving aztreonam.

Eighteen patients with hematological malignancies were studied. These patients received intravenous aztreonam instead of routine prophylactic antibiotics during the first week of their admission to a laminar-flow unit for the administration of cancer chemotherapy. Informed written consent was obtained from all patients. Patients with known allergies to penicillins or cephalosporins were not eligible for the study. Patients’ ages ranged from 16 to 65 years (mean, 48 years). The following laboratory values were required for entry into the study: serum creatinine <1.3 mg/dl, serum glutamic oxaloacetic transaminase <100 U/ml, and serum bilirubin <1.5 mg/dl. There were no changes in these laboratory values during aztreonam use.

Two dosage schedules were studied in these patients. One group of 9 patients received 1 g of aztreonam every 8 h for 7 to 9 days. Subsequently, another group of 9 patients received 2 g every 8 h for 7 to 9 days. The drug was administered in 50 ml of 5% dextrose solution over 30 min.

Two throat and two stool specimens were obtained for culture from each patient within the 4 days before aztreonam was started. Follow-up throat and stool cultures were collected twice, between days 3 and 5 and between days 7 and 9 of the aztreonam regimen.

Stool specimens were collected and placed immediately in a BBL GasPak Jar (BBL Microbiology Systems, Cockeysville, Md.). The specimens were inoculated directly onto 5% sheep blood agar (Remel, Lenexa, Kans.), LBS agar (BBL), Columbia CNA agar (Remel), Tergitol 7 agar H (Difco Laboratories, Detroit, Mich.), C. difficile isolation medium (Remel), Sabouraud dextrose agar (BBL) with gentamicin added, and thioglycolate broth (BBL). All cultures were incubated aerobically at 37°C, except for Lactobacillus and Clostridium difficile cultures, which were incubated anaerobically at 37°C.

Stool (5 g) was homogenized in 245 ml of sterile isotonic saline. Dilutions of 10-1, 10-3, 10-5, 10-6, and 10-7 were prepared from this stool homogenate, and serial dilutions were cultured on the previously described media for the isolation of aerobes. Serial dilutions were cultured anaerobically on 5% sheep blood agar (Remel), brucella agar (BBL), Columbia anaerobic neomycin blood agar (Remel), and C. difficile isolation medium (Remel).

Aerobic plates were incubated for 24 to 48 h, and organisms were identified by the methods of Edwards and Ewing (5) and Cowan and Steel (4). Anaerobic plates were read at 48 h, and isolates were identified by gas-liquid chromatography (8) and by biochemical reactions (Innovative Diagnostic Systems, Decatur, Ga.).

A semi-quantitative method was used for throat cultures (9). The patients gargled with 20 ml of sterile isotonic saline for 10 s and expectorated the specimen into a sterile container. Undiluted samples and dilutions of 10-1 to 10-5 were cultured on 5% sheep blood agar (Remel), LSB agar (BBL), Tergitol 7 agar H (Difco), Sabouraud dextrose agar (BBL) with gentamicin added, and Columbia CNA agar (Remel). Also, 1 ml of undiluted, gargled sample was cultured in thioglycolate broth (BBL). All cultures were incubated at 37°C with 5% CO2, except for Sabouraud and Tergitol plates, which were incubated without added CO2. Anaerobic cultures were not performed on throat specimens.

The effect of aztreonam on throat and stool flora was evaluated in the following manner. Only those organisms that were isolated from both of the throat cultures or both of the stool specimens obtained before aztreonam administration were considered in the analysis. Persistent organisms were defined as those that were isolated from specimens obtained before antibiotic administration and from the second follow-up specimen obtained during aztreonam administration.

Aztreonam had little effect on the predominant throat flora, such as streptococci and diphtheroids, when given in either of the two doses studied (Table 1). Aeromonas hydrophila was eliminated from the oropharynx of one patient, but Capnocytophaga spp. persisted in two of three carriers of this organism. No additional gram-negative bacilli were isolated from throat cultures. Seven of eight yeast isolates persisted in the throat during aztreonam prophylaxis.

Aztreonam caused a marked change in the fecal flora of the study patients (Table 2) receiving both regimens. The
Fungi

Bacteria were used in patients' prophylactic regimens. Bacilli, beta-lactam susceptible bacilli, and yeasts were selected. For example, aztreonam was administered to patients persisting with this flora on stool cultures. The number of bacterial isolates recovered from pretreatment stool cultures was surprisingly low. It was probably a result of prior use of prophylactic trimethoprim-sulfamethoxazole in these patients.

The effect of aztreonam on anaerobes was variable. The majority of isolates of Bacteroides spp. persisted during aztreonam administration, but three of three strains of Bacteroides fragilis were eliminated. The effect on Clostridium spp. was also variable. Eight of 12 strains isolated from patients receiving 2 g of aztreonam every 8 h were eliminated from the stool. None of the Clostridium spp. isolated during this study were identified as C. difficile. Six of six yeast isolates from stool cultures persisted during aztreonam use.

It was not possible to study the effect of aztreonam on the patients' susceptibility to the acquisition of resistant nosocomial bacteria or fungi, because these patients were housed in a laminar-flow unit and therefore were protected from nosocomial organisms. After discontinuation of aztreonam, other prophylactic antibiotics were employed; therefore, repopulation of the bowel flora could not be followed.

When compared with the effect of several of the newer beta-lactam antibiotics on bowel flora, aztreonam appears to spare some of the strict anaerobes, notably Bacteroides spp. For example, newer cephalosporins such as cefoperazone (1) and ceftriaxone (2) have led to a marked decrease in the number of strict anaerobes in the stool. The selective activity of aztreonam against aerobic, gram-negative bacilli suggests that this new monobactam may be useful in the treatment of immunocompromised patients.

**LITERATURE CITED**

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