Effectiveness of Aztreonam for the Treatment of Gonorrhea

ALAN GOTTLIEB AND JOHN MILLS*

Department of Medicine, University of California at San Francisco, and Medical Service, San Francisco General Hospital, San Francisco, California 94110

Received 29 May 1984/Accepted 6 November 1984

Aztreonam, 1 g intramuscularly, was compared with spectinomycin, 2 g intramuscularly, for uncomplicated gonorrhea. There were no failures with either drug. For aztreonam, there were 26 urethral, 3 rectal, and 3 endocervical sites that were infected. Aztreonam in a single dose of 1 g intramuscularly is satisfactory therapy for uncomplicated urethral gonorrhea in men and may be effective for rectal and endocervical infection as well.

Aztreonam is the first of a new class of beta-lactam antimicrobial agents, the monobactams. These agents have a monocyclic beta-lactam ring without the secondary ring found in penicillins and cephalosporins (1). Like these other beta-lactams, aztreonam kills susceptible organisms by interfering with synthesis of bacterial cell wall. Aztreonam has in vitro activity against gram-negative organisms such as the Enterobacteriaceae, Hemophilus influenzae, Pseudomonas spp., and Neisseria gonorrhoeae equivalent to that reported for the new third-generation cephalosporins (2-4, 8). All strains of N. gonorrhoeae, including those producing beta-lactamase, are highly susceptible to aztreonam (5). In humans the drug produces good serum levels with a half-life of about 1.5 h (10). We have studied the efficacy of aztreonam for uncomplicated gonococcal infection in humans.

Patients with microscopic or clinically diagnosed, or epidemiologic evidence of, gonococcal infections were selected from those visiting the San Francisco Department of Public Health Clinic for suspected sexually transmitted infections. Twelve women between the ages of 18 and 40 were treated who had evidence of epidemiological exposure to gonorrhea. Positive cultures for N. gonorrhoeae were obtained on six of those women. Seventy-five men between the ages of 18 and 55 with microscopically diagnosed urethral gonorrhea or evidence of rectal exposure to gonorrhea or both were also enrolled. Fifteen of those men were not evaluable because the pretreatment culture for N. gonorrhoeae was negative or because the patient failed to return for follow-up. No pharyngeal infections were diagnosed. Patients with a history of penicillin allergy, pregnancy, or serious underlying disease were excluded. Written informed consent was obtained in each case according to the guidelines of the University of California at San Francisco Committee on Human Research and U.S. Food and Drug Administration. The clinical or microscopic diagnosis of gonorrhea was confirmed by recovering oxidase-positive colonies of morphologically typical organisms on modified Thayer-Martin medium incubated at 35°C in 5% carbon dioxide. Rectal and cervical isolates were confirmed as N. gonorrhoeae by sugar utilization; this test was performed on urethral isolates only if the colony morphology was atypical. Isolates of N. gonorrhoeae were frozen at −70°C in Trypticase soy agar (BBL Microbiology Systems, Cockeysville, Md.) broth with 15% glycerol for subsequent susceptibility testing by agar dilution.

Patients were treated either with aztreonam alone, 1 g intramuscularly, or with spectinomycin, 2 g intramuscularly. The drugs were administered in a single-blind randomized fashion (only the patient was unaware of the material administered). Half of the patients were treated with aztreonam. Between 4 and 8 days after treatment, the patients returned to the clinic for replicate cultures of each infected site, which were processed as described above. At each visit, the following tests were obtained: complete blood count with differential, serum creatinine phosphokinase, creatinine, serum glutamic-oxaloacetic transaminase, bilirubin, alkaline phosphatase, blood urea nitrogen, urinalysis, and a serological test for syphilis.

Agar dilution susceptibility testing was performed according to the National Committee for Clinical Laboratory Standards Guidelines (6). Various concentrations of the antimicrobial agents being tested were prepared in a chocolate agar base, and an inoculum containing 5 × 10^6 CFU/ml was applied with a Steers replicator (9). Organisms with known susceptibility were included simultaneously as controls.

Both aztreonam and spectinomycin cured all patients treated. For aztreonam there were 26 urethral, 3 rectal, and 3 endocervical sites that were infected. For spectinomycin there were 25 urethral, 6 rectal, and 3 endocervical sites that were infected. With a total of about 30 patients treated with each drug and no failures, the 95% confidence limit of the true failure rate extends from 0 to 12%. No adverse reactions were observed that could be attributed to aztreonam. The intramuscular injections were well tolerated, with most patients complaining of mild burning at the site of injection for less than 15 min regardless of the drug used. No laboratory abnormalities could be attributed to either drug.

We tested 65 strains of N. gonorrhoeae recovered during this study for susceptibility to aztreonam and penicillin G (Table 1). The MIC of aztreonam for all but two strains was less than or equal to 0.12 mg liter. Those two strains had aztreonam MICs of 0.25 mg/liter. More than half of the strains were inhibited by 0.12 mg of penicillin per liter, but it required 0.5 mg/liter to inhibit over 90% of the strains, and one strain had a penicillin MIC greater than 2 mg/liter.

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>No. of strains</th>
<th>Cumulative % of strains susceptible at the following drug concn (mg/liter):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>≤ 0.01</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>65</td>
<td>20</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>65</td>
<td>17</td>
</tr>
</tbody>
</table>

* Corresponding author.
organism produced beta-lactamase and had an aztreonam MIC of 0.03.

Aztreonam in a single intramuscular dose of 1 g is effective, well tolerated, and safe therapy for uncomplicated gonococcal urethritis and is probably effective for endocervical and rectal infection as well. Similar results were obtained by Italian investigators (7). Because this drug is resistant to gonococcal beta-lactamase it would almost certainly be effective for penicillinase-producing Neisseria spp., and clinical studies to date have confirmed this (5). Although this agent is unlikely to replace existing agents for parenteral single-dose therapy of uncomplicated gonorrhea, it may be used in conjunction with other drugs for empiric treatment of conditions possibly due to the gonococcus (e.g., salpingitis, arthritis) where reliable antimicrobial activity toward the gonococcus is important.

The support of Erwin Braff and the physicians and staff of the San Francisco City Clinic is gratefully acknowledged. David Yajko is thanked for performing the bacteriology.

LITERATURE CITED