Single dose aztreonam in treating gonorrhoea

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SUMMARY Of 108 consecutive patients with urogenital gonorrhoea treated with a single 1 g intramuscular dose of aztreonam, 102 were suitable for evaluation. There was 100% cure at urogenital sites but treatment failed at three of 14 (21%) rectal or pharyngeal sites. In vitro resistance to aztreonam was not noted.

Introduction
Aztreonam is the first of a new class of β-lactam antibiotics, the monobactams, which have a novel monocyclic structure. The compound has a narrow range of activity directed against aerobic Gram-negative bacteria, is stable to most of the common Gram negative β-lactamases and, unlike many other β-lactam drugs, fails to induce the production of chromosomally mediated enzymes.†

The drug is not absorbed after oral administration and needs to be given parenterally. After a single 1 g intramuscular dose the mean serum concentration at one hour is 40 mg/l and the mean urine concentration at two hours is 1200 mg/l: the elimination half life of the drug is 1.3-2 hours.‡

The minimum inhibitory concentration of aztreonam for Neisseria gonorrhoeae, including β-lactamase producing strains, has been reported as 0·1-0·2 mg/l,¶ and the successful treatment of gonorrhoea with this drug has been reported.¶ For these reasons we undertook the study published here.

Patients, materials, and methods

CLINICAL
We studied 108 consecutive patients with urogenital gonorrhoea (80 men, 28 women) attending the genitourinary medicine clinic of this hospital. All patients were aged between 18 and 75: none gave a history of hypersensitivity to β-lactam drugs, were pregnant or lactating, or had received antimicrobial agents in the previous 14 days. Patients considered to be unlikely to attend for follow up at seven and 14 days were excluded by the clinical investigator. The treatment given was 1 g aztreonam in 3 ml water by deep intramuscular injection into the gluteal muscle.

LABORATORY
On entry to the trial a presumptive diagnosis of gonorrhoea was made by examining Gram stained smears from the urethra and cervix: in all patients included in the study the diagnosis was confirmed by the isolation of N gonorrhoeae. Rectal and oropharyngeal swabs from selected patients were cultured for N gonorrhoeae on a selective medium containing lincomycin, colistin, amphotericin B, and trimethoprim.

Urethral and cervical swabs from all patients were cultured in McCoy cells to isolate Chlamydia trachomatis. Saline mounted smears were made from all cervical swabs and examined for Trichomonas vaginalis: the swabs were also cultured on Sabouraud’s medium for Candida spp. All isolates of N gonorrhoeae were tested for β-lactamase production by the intralactam test strip method (Mast Laboratories, Bootle, England). Their sensitivity to penicillin and aztreonam was measured by an agar dilution method: plates of medium (Gibco GC agar base with 10% lysed blood) contained the appropriate antibiotic at five concentrations ranging from 0·06 mg/l to 1 mg/l and the inoculum was 10 colony forming units (cfu) of the test strain. Sensitivity to tetracycline, erythromycin, cefuroxime, and spectinomycin was tested by a standard disc diffusion method.

Results

CLINICAL
Of the 108 patients with urogenital gonorrhoea, 102 (74 men, 28 women) were suitable for evaluation: two who defaulted and four who had had sexual exposure during the follow up period, which may have resulted in reinfection, were excluded.
Men
On entry into the trial all 74 men had a purulent urethral discharge from which Neisseria gonorrhoeae was isolated and 33 (45%) were also infected with Chlamydia trachomatis. N gonorrhoeae was not isolated from cultures taken at the follow up visits seven and 14 days after treatment but 12 patients (16%), all with double infection, still complained of symptoms at the first of those visits. Gram stained films of urethral discharge from these 12 patients showed pus cells only and in each case Chlamydia trachomatis had been cultured from material taken at the initial visit. The patients were given a five day course of erythromycin and were symptomless by the time of their second return visit.

Women
Most of the 28 women were symptomless, though some had vaginitis. Most infected women attended as sexual contacts of male patients. Twelve had double infections: five with Trichomonas vaginalis, four with Candida albicans, and three with Chlamydia trachomatis. N gonorrhoeae was not isolated from any of the repeat urethral and cervical specimens taken at the seven and 14 day follow up visits.

Extragenital gonorrhoea
As well as having urogenital gonorrhoea, 14 patients had infection at extragenital sites (table I). Though a single dose of aztreonam rendered further cultures for N gonorrhoeae negative in 11 patients, positive cultures in the other three indicated persisting infection.

**TABLE I Patients with extragenital gonorrhoea cured by single 1 g dose of aztreonam**

<table>
<thead>
<tr>
<th>Sex</th>
<th>No cured/No infected at:</th>
<th>Rectum only</th>
<th>Pharynx only</th>
<th>Rectum and pharynx</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>5</td>
<td>1/1</td>
<td>1/2</td>
<td>1/2</td>
<td>3/5</td>
</tr>
<tr>
<td>Women</td>
<td>9</td>
<td>7/8</td>
<td>1/1</td>
<td></td>
<td>8/9</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>8/9</td>
<td>2/3</td>
<td>1/2</td>
<td>11/14</td>
</tr>
</tbody>
</table>

Adverse reactions
There were no appreciable side effects. One patient, a known alcoholic, complained of nausea and vomiting. Another patient who was incubating hepatitis B at the time of treatment subsequently developed jaundice, but made an uneventful recovery from his illness. The injection was well tolerated.

**LABORATORY**
The minimum inhibitory concentrations (MICs) of aztreonam for the isolates of N gonorrhoeae responsible for infection in the 102 patients ranged from less than 0.125 mg/l to 0.5 mg/l (table II). Only one isolate produced a β-lactamase (was a penicillinase producing strain of N gonorrhoeae (PPNG)): the MIC for that strain was 0.25 mg/l. The MICs for the isolates of N gonorrhoeae from extragenital sites before and after treatment in the three patients who failed to respond were 0.125 mg/l or less.

**TABLE II Activity of aztreonam against Neisseria gonorrhoeae isolated from 102 patients**

<table>
<thead>
<tr>
<th>No of isolates</th>
<th>Minimum inhibitory concentrations (mg/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>69</td>
<td>&lt;0.125</td>
</tr>
<tr>
<td>26</td>
<td>0.125</td>
</tr>
<tr>
<td>5</td>
<td>0.25</td>
</tr>
<tr>
<td>2</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Discussion
One hundred and two patients infected with Neisseria gonorrhoeae at urogenital sites were cured by a single 1 g dose of aztreonam. Cultures taken from the urethra (men) or the urethra and cervix (women) seven and 14 days after treatment were negative. Clinical response was good except in 12 of the 74 men, who still complained of urethral discharge at seven days and had evidence of concurrent infection with Chlamydia trachomatis. These symptoms responded to erythromycin.

This cure rate of 100% is exceptionally good because various treatment regimens for gonorrhoea fail in 2-5% of patients. McLean and Harris reported successful treatment in 62 of 65 patients (95%) with uncomplicated gonorrhoea given a single 1 g dose of aztreonam:4 their three failures were in men with urethral infection, but each of the 10 patients with extragenital infections (eight rectal, two pharyngeal), which are generally regarded as more difficult to treat, responded. In the series published here infection persisted in three of 14 patients (21%) who had infection of the rectum or pharynx. Resistance in vitro was not found in any of the isolates of N gonorrhoeae, and treatment failure was not associated with any decrease in sensitivity. A single patient infected with a PPNG strain was cured: a high (14%) proportion of the organisms isolated by McLean and Harris were β-lactamase producers, and all infections caused by them responded.4 Though infections caused by PPNG strains are still unusual in the west of Scotland, they are common elsewhere and some spectinomycin resistant strains have been encountered.

Aztreonam, a well tolerated β-lactam antibiotic, seems to be a useful addition to the drugs that can be used for successful single dose treatment of
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gonorrhoea, especially when the infecting strain is resistant to other agents.

We thank ER Squibb and Sons for the supply of aztreonam.

References


