TREATMENT OF GONORRHEA: COMPARISON OF CEFOXITIME AND PENICILLIN

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Ninety-seven patients with 118 sites infected with Neisseria gonorrhoeae were treated with a single dose of either procaine penicillin G (4.8 × 10^6 U) or cefoxitine (1.0 g) intramuscularly. Only the penicillin group took 1 g of probenecid orally. The numbers of infected sites in each treatment group were as follows: penicillin—urethra, 37; rectum, 9; cervix, 8; and pharynx, 4; cefoxitine—urethra, 42; rectum, 9; cervix, 5; and pharynx, 4. The cure rates in each treatment group were 100%. No adverse reactions were noted in either group. Beta-lactamase-positive N. gonorrhoeae strains were not found. Ninety-five percent of clinical isolates were inhibited by ≤0.007 µg of cefoxitine and ≤0.25 µg of penicillin per ml. In this study cefoxitine was as effective as procaine penicillin in the treatment of uncomplicated gonorrhea.

Cefoxitine, a semisynthetic cephalosporin, has shown excellent activity against Neisseria gonorrhoeae, including strains which produce beta-lactamase (1, 8). It was noted to be more active than a variety of other antimicrobial agents in vitro on a per-weight basis (8). The minimum inhibitory concentration of cefoxitine remained the same (≤0.004 µg/ml) whether beta-lactamase was produced or not (1). The mean peak serum concentration of cefoxitine after a 1.0-g intramuscular (i.m.) injection has been reported to be 20.5 µg/ml, with a half-life of 1.34 h (4). Recently, in a noncomparative clinical trial in Europe, cefoxitine was found to be highly effective against gonococcal urethritis and cervicitis (5). We undertook this study to compare the efficacy and safety of cefoxitine with that of penicillin in the single-dose treatment of uncomplicated gonococcal infections.


MATERIALS AND METHODS

Patient selection. All patients were seen between November 1979 and May 1980 at the Venerable Disease Clinic affiliated with Hennepin County Medical Center. Men were accepted to the study if urethral smears revealed gram-negative intracellular diplococci or if previous cultures were positive. Women who were known gonorrhea contacts or who had previous positive cultures were eligible for the study. Informed, written consent was obtained from all patients participating in the study. Reasons for exclusion from the study were presence of a known systemic disease, evidence of disseminated gonococcal infection, usage of antibiotics in the previous 10 days, or history of allergy to penicillins, cephalosporins, or probenecid. Women with evidence of pelvic inflammatory disease were also excluded.

Treatment and follow-up. Patients were assigned to one of the two treatment groups according to an allocation schedule of random numbers. The first regimen consisted of 1 g of cefoxitine reconstituted with 3.0 ml of sterile water administered as one i.m. injection. The alternate regimen was 4.8 × 10^6 U of aqueous procaine penicillin i.m. as two injections plus 1.0 g of probenecid orally. After examination by a physician, the participants were treated. Re-evaluation and test of cure cultures were obtained 3 to 7 days after treatment. Participants were asked to refrain from sexual intercourse between the time of treatment and follow-up evaluation.

Laboratory methods. All culture specimens were immediately inoculated on Thayer-Martin media and were incubated at 35°C and under 5% CO2. Colonies of N. gonorrhoeae were identified by typical morphological appearance, Gram stain, positive oxidase test, and carbohydrate utilization tests. N. gonorrhoeae isolates were tested for beta-lactamase by an acidimetric method (9). Heavy suspensions of pure cultures were made in Trypticase soy broth (BBL Microbiology Systems, Cockeysville, Md.) containing 20% glycerol and immediately frozen at −70°C for future use.

Cefoxitine was obtained from Hoechst-Roussel Pharmaceuticals, Inc., Somerville, N.J., and penicillin G was obtained from Wyeth Laboratories, Philadelphia, Pa.
The minimum inhibitory concentrations of penicillin and cefotaxime for the clinical isolates were determined by the agar dilution technique (6).

Pre- and posttreatment laboratory tests included complete blood counts with platelet estimate, urinalysis, blood urea nitrogen, creatinine, alkaline phosphatase, serum glutamic pyruvic transaminase, bilirubin, and serology for syphilis.

RESULTS

A total of 126 patients were enrolled in the study. Sixteen patients with sterile pretreatment cultures and 13 patients who did not return for follow-up were excluded. Of the remaining 97 patients, 45 males and 5 females were in the cefotaxime group and 39 males and 8 females were in the penicillin group. Age, race, and duration of symptoms in the two groups were similar. The total number of infected sites was 118.

Results of the two treatment groups are summarized in Table 1. Cure rates in both groups at all infected sites were 100%.

Two men who received cefotaxime continued to have a discharge at the follow-up visit. Gram stain was negative for gonococci, and cultures were also negative. The patients were treated for postgonococcal urethritis.

No adverse side effects were noted in either treatment group. Cefotaxime administered as a single i.m. injection was better accepted by patients and easier to administer than penicillin, which was administered in two i.m. injections. Cefotaxime was injected without lidocaine. Grading of pain at the injection site in 50 patients treated with cefotaxime and 47 patients treated with penicillin was as follows: cefotaxime—no pain, 20; mild pain, 27; and moderate pain, 3; penicillin—no pain, 14; mild pain, 26; and moderate pain, 7. No significant changes in the pre- and posttreatment laboratory tests were noted in either treatment group.

The minimum inhibitory concentrations of cefotaxime and penicillin were determined for 131 N. gonorrhoeae isolates from this study population. Ninety-five percent of clinical isolates were inhibited by ≤0.007 μg of cefotaxime and 0.25 μg of penicillin per ml (Fig. 1). No β-lactamase-positive N. gonorrhoeae strains were noted in this study.

DISCUSSION

For over 30 years, penicillin has been one of the primary antimicrobial agents used in the single-dose treatment of gonorrhea. During this period the susceptibility of gonococci to penicillin has decreased (7). Presently, the treatment of gonorrhea with penicillin includes two i.m. injections (2.4 × 10^6 U each) plus 1 g of oral probenecid. Any further increase in the dose of penicillin would require administration of three i.m. injections, which would make penicillin treatment undesirable for many patients. Furthermore, standard high-dose penicillin therapy does not eradicate infection due to β-lactamase-positive N. gonorrhoeae (3). This has prompted a search for new antimicrobial agents for the single-dose treatment of gonorrhea.

Several new cephalosporins and cephemycin antimicrobial agents have excellent in vitro activity against N. gonorrhoeae, including β-lactamase-positive strains (8). Recent clinical studies concerning the use of these new anti-microbial agents in gonococcal infections have shown encouraging results. Cefoxitin, a cephemycin antimicrobial agent, has been shown to be effective in infections due to β-lactamase-negative and β-lactamase-positive N. gonorrhoeae (2, 10). Cefotaxime is currently undergoing clinical trials in gonococcal infections. Cure rates of over 96% in approximately 100 patients treated with cefotaxime for uncomplicated gonorrhea have been reported. (H. H. Handsfield and K. K. Holmes, 20th ICAAC, abstr. no. 317, 1980; B. Lutz, B. Pauling, J. Kosola, and W. J. Mogabgab, 20th ICAAC, abstr. no. 67, 1980). As predicted by in vitro studies (1, 8), cefotaxime has also been

![Fig. 1. Comparison of the minimum inhibitory concentrations of cefotaxime and penicillin for 131 N. gonorrhoeae strains isolated from the study population.](http://aac.asm.org/)

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**TABLE 1. Treatment results with 97 patients (118 infection sites)**

<table>
<thead>
<tr>
<th>Infection site</th>
<th>Cefotaxime group</th>
<th>Penicillin group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urethra</td>
<td>42/42</td>
<td>37/37</td>
</tr>
<tr>
<td>Cervix</td>
<td>5/5</td>
<td>8/8</td>
</tr>
<tr>
<td>Rectum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>6/6</td>
<td>3/3</td>
</tr>
<tr>
<td>Females</td>
<td>3/3</td>
<td>6/6</td>
</tr>
<tr>
<td>Pharynx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>3/3</td>
<td>3/3</td>
</tr>
<tr>
<td>Females</td>
<td>1/1</td>
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</tr>
</tbody>
</table>

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**FIG. 1. Comparison of the minimum inhibitory concentrations of cefotaxime and penicillin for 131 N. gonorrhoeae strains isolated from the study population.**

In this study, cefotaxime was as effective as procaine penicillin in the treatment of uncomplicated gonorrhea. All infected sites were uniformly cured in both treatment groups. However, when compared with gonococcal urethritis, only a small number of cervical, rectal, and pharyngeal gonococcal infections have been treated. Further clinical trials are needed to verify the efficacy of cefotaxime against infections of these latter sites.

In conclusion, cefotaxime appears to be an effective antimicrobial agent in treating gonococcal urethritis caused by β-lactamase-negative strains. Concomitant oral probenecid is not needed for cefotaxime efficacy in gonorrhea treatment.

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LITERATURE CITED


