Comparative Efficacy of Cefmenoxime Versus Penicillin in the Treatment of Gonorrhea

STEPHEN R. OBAID,1 MOHAMMED Y. KHAN,1,4 MARGARET L. SIMPSON,1 ROBERT P. GRUNINGER,2 AND DAVID I. WIGREN3

Department of Medicine, Section of Infectious Diseases,1 Departments of Pathology2 and Obstetrics-Gynecology,3 Hennepin County Medical Center, University of Minnesota Medical School, Minneapolis, Minnesota 55415

Received 27 September 1982/Accepted 14 December 1982

A total of 121 men with complicated infections caused by β-lactamase-negative Neisseria gonorrhoeae were included in this study. They were randomly assigned to regimens of either cefmenoxime (1.0 g) or procaine penicillin G (4.8 × 10^6 U) intramuscularly. Only the penicillin group also took 1.0 g of probenecid orally. A total of 99 patients completed the study, providing data from 108 infected sites. In the cefmenoxime group, there were 49 urethral, 1 rectal, and 2 pharyngeal infections; in the penicillin group, there were 49 urethral, 4 rectal, and 3 pharyngeal infections. In the cefmenoxime group, all except one urethral infection were eradicated. This patient admitted having had sexual intercourse during the follow-up period and was considered to be reinfected. In the penicillin group, all except one pharyngeal infection were cured. No adverse reactions were noted in either group. In this study, cefmenoxime was as effective as penicillin in the treatment of gonococcal urethritis in men.

Cefmenoxime (SCE-1365, A-50912), a new semisynthetic cephalosporin antimicrobial agent, is highly active in vitro against Neisseria gonorrhoeae (6). It inhibits all isolates, regardless of β-lactamase activity, at a concentration of 0.015 μg/ml (6). The peak serum concentration of cefmenoxime after a 1.0-g intramuscular (i.m.) injection has been reported to be 24.0 ± 2.1 μg/ml, with a half-life of 99.6 ± 7.3 min (J. Guibert, M. D. Kitzis, C. Yvelin, L. Petrescu, and A. Bryskier, Program Abstr. Intersci. Conf. Antimicrob. Agents Chemother. 21st, Chicago, Ill., abstr. no. 606, 1981). In this study, we compared the efficacy and safety of cefmenoxime with those of penicillin in the single-dose treatment of uncomplicated gonococcal infections. To our knowledge, clinical studies to assess the efficacy of cefmenoxime in the treatment of gonorrhea have not been previously reported.

MATERIALS AND METHODS

Patient selection. All patients were seen between September 1981 and August 1982 at the venereal disease clinic affiliated with Hennepin County Medical Center, Minneapolis, Minn. Male patients with suspected gonococcal urogenital infections were solicited for entry into this study. Patients were accepted for participation in the study if urethral smears revealed gram-negative intracellular diplococci or if previous cultures were positive. Informed written consent was obtained from all participating patients. Reasons for exclusion from the study were presence of serious underlying disease; evidence of syphilis or disseminated gonococcal infection; known allergies to penicillin, cephalosporins, lidocaine, or probenecid; or the presence of any other disease requiring concomitant antimicrobial therapy.

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 1.0 g of cefmenoxime reconstituted with 3.6 ml of either sterile water or 0.5% lidocaine administered as one i.m. injection into the gluteal muscle mass. The alternate regimen was 4.8 × 10^6 U of aqueous procaine penicillin given i.m. as two injections plus 1.0 g of probenecid orally. After examination by a physician, the participants were treated. Cultures from the urethra and pharynx of each patient were tested for N. gonorrhoeae. In addition, rectal cultures from 22 homosexual men were tested. 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 medium and then incubated at 35°C in an atmosphere with air and 5% CO₂. N. gonorrhoeae colonies were identified by typical morphological appearance, Gram stain, positive oxidase test, and carbohydrate utilization tests. N. gonorrhoeae isolates were tested for β-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 stored at −70°C for future use.
Cefmenoxime was obtained from Abbott Laboratories, North Chicago, Ill., and penicillin G was obtained from Wyeth Laboratories, Philadelphia, Pa. The minimal inhibitory concentrations of cefmenoxime and penicillin for 126 clinical isolates from the study population were determined by the agar dilution technique (5).

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

RESULTS

Of the 121 men enrolled in the study, 14 who did not return for follow-up examination and 8 with sterile pretreatment cultures were excluded. Of the remaining 99 patients, 50 were treated with cefmenoxime and 49 received penicillin. Age, race, and duration of symptoms were comparable in the two groups. The total number of infected sites was 108. Results of the two treatment groups are summarized in Table 1. In the cefmenoxime group, all except one urethral infection were eradicated. This patient admitted having had sexual intercourse between the time of treatment and the follow-up evaluation. This case was considered to be a reinfection and not a treatment failure. Cefmenoxime cured the single rectal and the two pharyngeal infections. After therapy with cefmenoxime for a urethral infection, one patient returned with a positive pharyngeal culture which had been sterile on the initial visit. In this patient, oral sexual exposure between the two visits could not be excluded with certainty. Penicillin cured all 49 urethral infections and the 4 rectal infections. However, one of the three pharyngeal infections was not eradicated by penicillin. This patient denied having had sexual activity during the follow-up period. No β-lactamase-positive *N. gonorrhoeae* strains were found in this study.

No adverse side effects were noted in either treatment group. Eight men in the cefmenoxime group and three in the penicillin group returned with urethral discharge. These patients had sterile cultures for *N. gonorrhoeae* and were treated for postgonococcal urethritis. Cefmenoxime was reconstituted with sterile water for injection in the first 17 patients. It caused more pain at the injection site than did penicillin. Subsequent patients received cefmenoxime with lidocaine, which was better tolerated than cefmenoxime without lidocaine. Addition of lidocaine to cefmenoxime resulted in discomfort similar to that observed after procaine penicillin. No significant changes in the pre- and posttreatment laboratory tests were noted in either treatment group.

The minimal inhibitory concentrations of cefmenoxime and penicillin were determined for 126 *N. gonorrhoeae* isolates from this study population. Ninety percent of the clinical isolates were inhibited by ≤0.01 μg of cefmenoxime and ≤0.32 μg of penicillin per ml (Fig. 1).
DISCUSSION

The Centers for Disease Control, Atlanta, Ga., continues to recommend a single dose of procaine penicillin G as one of the initial treatments of choice for uncomplicated gonorrhea (1). However, with the worldwide emergence of β-lactamase-positive N. gonorrhoeae (2), newer antimicrobial agents are being sought for infections caused by these penicillin-resistant strains.

Several new β-lactam antimicrobial agents have excellent in vitro activity against N. gonorrhoeae, including β-lactamase-positive strains (8, 10, 11). Recent clinical studies concerning the use of these new antimicrobial agents in gonococcal infections have shown encouraging results (3, 4, 7).

In this study, cefmenoxime was as effective as procaine penicillin in the treatment of gonococcal urethritis. The fact that only a single i.m. injection of cefmenoxime was required, in contrast to the two i.m. injections required with penicillin, was considered to be an advantage by both patients and health workers. Furthermore, concomitant oral probenecid was not required for cefmenoxime efficacy in gonorrhea treatment.

A very small number of rectal and pharyngeal gonococcal infections were treated in this study. Although cefmenoxime cured these infected sites, further clinical trials are needed before conclusions can be drawn.

All of the infections in this study were caused by β-lactamase-negative N. gonorrhoeae. When compared with penicillin, cefmenoxime showed 32-fold greater in vitro activity against these isolates. Cefmenoxime has also been shown to be highly active in vitro against β-lactamase-positive N. gonorrhoeae (6).

In summary, cefmenoxime appears to be an effective antimicrobial agent in treating gonococcal urethritis caused by β-lactamase-negative strains. Clinical trials to verify the efficacy of cefmenoxime in treating β-lactamase-positive N. gonorrhoeae infections are indicated.

ACKNOWLEDGMENTS

This investigation was supported by a grant from Abbott Laboratories and TAP Pharmaceuticals, North Chicago, Ill.

We acknowledge the assistance of the personnel at the Red Door Clinic, Hennepin County Medical Center, and are grateful to Susan Nelson for technical assistance and to Rosemary Pellegini for typing the manuscript.

LITERATURE CITED


