Dose-Ranging Study of Ceftriaxone for Uncomplicated Gonorrhea in Men

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Uncomplicated gonorrhea in men was successfully treated with ceftriaxone in single intramuscular doses of 125 mg (15 patients), 250 mg (16 patients), or 500 mg (15 patients). All 45 pretreatment gonococcal isolates tested were inhibited by \( \leq 0.016 \mu g/ml \) of ceftriaxone per ml. Treatment was well tolerated and caused no toxicity.

The increasing prevalence of beta-lactamase-producing strains of *Neisseria gonorrhoeae* (3, 7) and various disadvantages of the regimens recommended by the U.S. Centers for Disease Control (2) for gonorrhea due to beta-lactamase-negative strains have stimulated investigation of newly developed antimicrobial agents for the treatment of uncomplicated gonorrhea. Ceftriaxone (Ro 13-9904) is a new cephalosporin that possesses unique pharmacokinetic properties, with a mean peak serum level of 93 \( \mu g/ml \) and a serum half-life of 8 h after a single intravenous dose of 500 mg (8), and is one of the most active of all antibiotics against both beta-lactamase-positive and -negative *N. gonorrhoeae* (minimal inhibitory concentration [MIC] usually \( \leq 0.008 \mu g/ml \)) (4-6, 9, 11). These features suggest that ceftriaxone has potential value as a single-dose treatment for uncomplicated gonorrhea. We undertook a randomized dose-ranging study to assess the efficacy and tolerance of single intramuscular doses of 125, 250, or 500 mg of ceftriaxone in men with uncomplicated urethral or anorectal infection with beta-lactamase-negative *N. gonorrhoeae*.

Fifty-three men aged \( \geq 16 \) years who attended a sexually transmitted disease clinic and who had presumptive gonococcal urethritis (urethral smear showing intracellular gram-negative diplococci) or anorectal infection (positive Gram-stained smear or history of receptive rectal intercourse with a man with documented gonococcal urethritis) were enrolled in the study after giving written informed consent. Patients with histories of allergy to beta-lactam antibiotics, with complications of gonorrhea, or who had received antimicrobial therapy within the preceding 2 weeks were excluded. Ceftriaxone was dissolved in 1% lidocaine and administered in single intramuscular doses of 125 mg (0.5 ml), 250 mg (1.0 ml), or 500 mg (2.0 ml) according to a computer-generated randomization schedule provided by the manufacturer. Gonococcal infection was confirmed by the isolation of *N. gonorrhoeae* from 52 men, 46 of whom returned for follow-up examinations 3 to 8 days after treatment. Success or failure of treatment was defined by the results of cultures for *N. gonorrhoeae* at the follow-up visit. Complete blood counts, platelet counts, urinalyses, blood urea nitrogen, prothrombin time, and serum creatinine, creatine phosphokinase, glutamic-oxalactic transaminase, and total bilirubin assays were performed by routine methods before treatment and at the follow-up visit.

Urethral, anal canal, and pharyngeal specimens were obtained with swabs from all patients at each visit and were directly inoculated onto modified Thayer-Martin medium, which was incubated within 30 min at 36°C in a candle extinction jar. *N. gonorrhoeae* was identified by routine methods, including sugar utilization profiles. Isolates were stored by freezing at \(-70°C\) in a 1:1 mixture (vol/vol) of horse serum and tryptic soy-yeast broth for later antimicrobial susceptibility testing. The MICs of ceftriaxone, penicillin G, and tetracycline were determined for pretreatment gonococcal isolates from 45 patients by an agar dilution technique (10), using twofold dilutions of antibiotic in gonococcal agar base (BBL) containing 1% concentrations of IsoViteX (BBL) and hemoglobin. One isolate, from the urethra or anal canal, was tested for each patient. Beta-lactamase production was tested by the iodometric method (1).

The mean age \( \pm \) one standard deviation of the 46 infected patients who returned for follow-up examination was 26.9 \( \pm \) 7.7 years (range, 16 to
infections at penicillin G, and was treatment no with the even strains of normal tests were found to be infected at the follow-up visit. No significant hematological, urinary, or biochemical abnormalities occurred, except that anicteric viral hepatitis was documented before treatment in two men. In these cases, the hepatic function tests were unchanged or had returned toward normal at the follow-up visit.

Table 1 shows the in vitro susceptibility of 45 strains of N. gonorrhoeae isolated in this study. The geometric mean MICs of ceftriaxone, penicillin G, and tetracycline were 0.0043 µg/ml, 0.29 µg/ml, and 0.50 µg/ml, respectively. All isolates gave negative tests for beta-lactamase.

Ceftriaxone is a promising drug for single-dose treatment of uncomplicated gonorrhea. N. gonorrhoeae was eradicated from all infected sites, even with the 125-mg dose, and treatment caused no perceptible toxicity. The drug is readily soluble and could be injected through small-gauge needles; intramuscular injection of ceftriaxone in 1% lidocaine into the deltoid muscle was virtually painless. The in vitro susceptibility of N. gonorrhoeae to ceftriaxone in this study is consistent with that reported previously (4–6, 9, 11); moreover, beta-lactamase-producing strains have been reported (6, 11) to be as susceptible as beta-lactamase-negative strains. Thus, ceftriaxone in doses of 125 to 500 mg should be studied in controlled trials to compare its efficacy with that of established regimens for uncomplicated gonorrhea due to beta-lactamase-positive or -negative N. gonorrhoeae.

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**LITERATURE CITED**