NOTES

Comparison of Ofloxacin and Ceftriaxone in the Treatment of Uncomplicated Gonorrhea Caused by Penicillinase-Producing and Non-Penicillinase-Producing Strains

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Eighty-nine patients with uncomplicated gonorrhea, including 31 patients (34.8%) infected with penicillinase-producing strains of Neisseria gonorrhoeae, were treated with oral ofloxacin (single 400 mg dose) or intramuscular ceftriaxone (250-mg dose). All 47 patients who received ofloxacin and 41 of 42 patients who received ceftriaxone were cured.

The increasing prevalence of penicillinase-producing Neisseria gonorrhoeae and of strains with chromosomal resistance to penicillin and alternative drugs like spectinomycin (1, 8) has made it necessary to evaluate other agents in the treatment of gonorrhea.

Ofloxacin is a synthetic fluorinated carboxyquinolone that has a broad spectrum of activity against both gram-negative and gram-positive bacteria. It exerts its antimicrobial effect by inhibition of the essential microbial enzyme DNA gyrase. Quinolones have high in vitro activity against gonococci (2, 9). Both norfloxacin and ciprofloxacin have been successfully used to treat uncomplicated urethral gonorrhea in men (6, 7, 14). Cure rates of up to 100% have been reported in previous single-dose studies of ofloxacin in the treatment of gonococcal infection (3, 5, 13).

Patients were studied at the New York City Department of Health Crown Heights Sexually Transmitted Disease Clinic in Brooklyn, N.Y., between March and July 1988. Heterosexual men or women at least 18 years old were eligible for study participation. Male participants had a urethral Gram stain showing gram-negative intracellular diplococci. Female participants had a known positive culture, a cervical Gram stain showing gram-negative intracellular diplococci, or recent exposure to a man with documented gonorrhea. Pregnant or nursing women; patients with a history of allergic reaction to carboxyquinolones, nalidixic acid, ceftriaxone, or cephalosporins; and patients who had received systemic antimicrobial therapy within the previous 24 h were excluded. All patients provided written informed consent.

Specimens for culture were obtained from the male urethra or from the endocervix and from the pharynx and the anal canal. Specimens were inoculated directly onto modified Thayer-Martin agar or onto New York City agar and incubated in candle jars at 36°C for 24 to 48 h. Isolates were identified as N. gonorrhoeae by using Gram stain, oxidase reaction, and Gonochek II microbial identification tubes (Du Pont Co., Wilmington, Del.). Production of β-lactamase was detected by nitrocefin (Cefinase) disks (BBL Microbiology Systems, Cockeysville, Md.) (10, 12). Isolates of N. gonorrhoeae were stored at −70°C in 15% glycerol in Mueller-Hinton broth. MICs of ofloxacin and ceftriaxone were determined by the agar dilution method on GC agar base (Difco Laboratories, Detroit, Mich.) containing 1% IsoVitaleX (BBL), 1% hemoglobin, and twofold dilutions of each drug. Cultures for Chlamydia trachomatis were obtained by passing sterile type I cotton swabs (Spectrum Laboratories, Houston, Tex.) into the male urethra or the endocervix. The swabs were immediately placed into 0.55 ml of sucrose-phosphate-glutamate transport medium and frozen at −70°C for later inoculation onto McCoy cell monolayers. Inoculated cultures were incubated at 35 to 37°C for at least 65 h, stained with iodine, and examined for inclusions.

After all appropriate smears and cultures were obtained, patients were randomly assigned to be treated with either 400 mg of oral ofloxacin or 250 mg of intramuscular ceftriaxone. Patients were asked to return 4 to 8 days after treatment and to refrain from sexual activity until the follow-up visit. During the posttreatment visit, patients were examined and questioned about side effects. Test-of-cure cultures were obtained from the same sites cultured before treatment.

Fifty-four men and fifty women were enrolled in the study. Of the 54 men with uncomplicated urethral gonococcal infection, 52 returned for the posttreatment visit and could thus be evaluated. Of the 50 enrolled women, 9 were excluded because N. gonorrhoeae was not isolated from the pretreatment culture, and 4 failed to appear for the posttreatment visit. Isolates from 31 of the 89 patients who could be evaluated (34.8%) produced penicillinase.

The results of treatment are presented in Table 1. All 47 patients who were treated with ofloxacin, including 16 whose isolates of N. gonorrhoeae produced penicillinase, were cured. Four patients reported mild gastrointestinal side effects including nausea and diarrhea, three noted drowsiness, and two female participants developed symptomatic posttreatment vulvovaginal candidiasis. Forty-two patients, including fifteen with penicillinase-producing N. gonor-
rheae, received ceftriaxone. In the one treatment failure, penicillinase-producing *N. gonorrhoeae* was isolated from the anorectal culture of the patient before treatment and at the follow-up visit. This patient denied intersexual contact and had no symptoms at the follow-up. Two patients who received ceftriaxone complained of nausea and diarrhea, and one reported drowsiness.

MICs of ofloxacin and ceftriaxone were determined for the 89 patients who could be evaluated. The geometric mean MIC for penicillinase-producing isolates was 0.01 µg/ml (range, 0.004 to 0.03 µg/ml) for ofloxacin and 0.006 µg/ml (range, 0.002 to 0.008 µg/ml) for ceftriaxone, while for non-penicillinase-producing isolates these values were 0.01 and 0.005 µg/ml, respectively, with the same ranges.

Chlamydial cultures were done with specimens from the 89 participants who could be evaluated. *C. trachomatis* was isolated from pretreatment cultures from one man and four women who received ofloxacin and from two men and three women who received ceftriaxone. Posttreatment cultures from 9 of the 10 infected patients contained *C. trachomatis*. In addition, for one male participant whose pretreatment chlamydial culture was contaminated, *C. trachomatis* was recovered from posttreatment specimens.

This study demonstrated that a single oral dose of 400 mg of ofloxacin was highly effective in the treatment of uncomplicated infections due to penicillinase-producing and non-penicillinase-producing strains of *N. gonorrhoeae*.

Single-dose ofloxacin, like other quinolones, does not seem to have any effect against *C. trachomatis*, although longer courses of ofloxacin appear to be effective in eradicating *C. trachomatis* (4, 11). Therefore, when single-dose quinolones are used to treat gonorrhea, a 7-day course of doxycycline or erythromycin also should be prescribed.

Quinolones such as ofloxacin offer advantages such as ease of administration, good acceptance by patients, low toxicity, activity against penicillinase-producing *N. gonorrhoeae*, and reduced cost. Possible disadvantages for the use of quinolones for treatment of gonorrhea are that (i) they are contraindicated in women who may be pregnant; (ii) the effect of quinolone treatment on incubating syphilis is not known, although ofloxacin had little or no activity against *Treponema pallidum* in a rabbit model (16); and (iii) there is a potential in the gonococcus for single-step, high-level resistance to quinolones (15). Quinolones should eventually become useful for the treatment of gonococcal infections, unless the gonococci develop resistance to the treatment.

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**LITERATURE CITED**