

## NOTES

# Comparative Clinical Efficacy of Single Oral Doses of Cefuroxime Axetil and Amoxicillin in Uncomplicated Gonococcal Infections

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**Cefuroxime axetil (1.5 g) was compared with amoxicillin (3 g), both given as a single oral dose combined with probenecid (1 g) for the treatment of uncomplicated gonorrhoea. Of 60 evaluable patients receiving amoxicillin, 55 (91.7%) were cured, whereas 55 (96.5%) of the 57 patients receiving cefuroxime axetil were cured ( $P > 0.1$ ). Both drugs were well tolerated.**

Cefuroxime axetil (the prodrug of cefuroxime), when given orally, produces an adequate concentration of cefuroxime in serum for 8 h, with peak concentrations averaging 8.6 mg/liter 2 h after a 500-mg dose (11). The parenteral cefuroxime has been shown to be effective as a single dose in gonococcal (GC) infections (9) and is relatively resistant to various  $\beta$ -lactamase enzymes (8, 12). Cefuroxime axetil was thus compared with amoxicillin in patients with uncomplicated GC infections.

Patients attending the Venereal Disease Clinic at St. Michael's Hospital with uncomplicated GC infection of the urethra or cervix were enrolled in a prospective, randomized single-blind study. Informed, written consents were obtained from all patients. At assessment, calcium alginate swabs were taken from the urethra and endocervix for Gram stains and were plated onto Thayer-Martin and New York City media. Homosexual patients or patients with oral or anal contact had swabs taken from the pharynx and anorectal area for GC cultures on Thayer-Martin media (containing vancomycin, colistin, and nystatin). Patients with suspected or proven oropharyngeal infection, pelvic inflammatory disease, or disseminated GC infections were excluded from the study.

Patients were randomized to receive cefuroxime axetil (1.5 g) with 1 g of probenecid or 3 g of amoxicillin with 1 g of probenecid, all given as single oral doses. The medications were provided in a sealed carton with only the allocation numbers visible. The medication was administered by nurses, but the attending physicians were unaware of the medication received. Patients were reassessed for test of cure 1 to 2 weeks posttreatment. Cure of infection was defined as resolution of symptoms and signs with negative smear and culture on first follow-up.

Post-GC urethritis was defined as improvement with reappearance of symptoms and signs but negative cultures for gonorrhoea. However, chlamydia cultures were not done, and in view of the short follow-up, the incidence of post-GC urethritis was inadequately assessed. All GC strains were tested for  $\beta$ -lactamase production by the paper strip method (Oxoid Ltd., London, England). Susceptibility testing was done by the agar dilution method (4), using GC agar base

with 1% IsoVitaleX (BBL Microbiology Systems, Cockeysville, Md.) and 1% hemoglobin, and  $10^4$  CFU were spotted with a Steers replicator. Typical oxidase-positive colonies with gram-negative diplococci were identified as *Neisseria gonorrhoeae* by the ability to ferment glucose but not sucrose, lactose, or maltose.

A total of 150 patients were enrolled in the study, 76 receiving amoxicillin and 74 receiving cefuroxime axetil; 30 patients (15 from each group) failed to return for follow-up and were excluded. Three other patients were excluded from analysis, one of whom had received another antibiotic before reassessment, and two others were late for first follow-up (over 1 month posttreatment). There were 117 evaluable patients, 60 receiving amoxicillin and 57 receiving cefuroxime (Table 1). There were 13 evaluable women, 7 receiving amoxicillin and 6 receiving cefuroxime. Of the evaluable patients receiving amoxicillin, 55 (91.7%) were symptomatic, whereas 50 (87.7%) of the patients receiving cefuroxime had symptoms. The asymptomatic patients either had sexual contacts with known cases of gonorrhoea or with prostitutes. None of the patients in either group had gonococci isolated from oropharyngeal or anorectal swabs.

Of the 60 evaluable patients receiving amoxicillin, 55 (91.7%) were cured of their GC infection, with 5 (8.3%) treatment failures. Two homosexual men in this group were cured of their infections. One of the seven women receiving amoxicillin was a treatment failure. Five patients (8.3%) had post-GC urethritis at 1 to 2 weeks follow-up.

TABLE 1. Summary of results of treatment with cefuroxime axetil versus amoxicillin in uncomplicated GC infections

Patient status	No. of patients (% <sup>a</sup> )	
	Amoxicillin	Cefuroxime axetil
Enrolled	76	74
Excluded from analysis	16	17
Evaluable	60	57
Cured	55 (91.7)	55 (96.5)
Treatment failure	5 (8.2)	2 (3.5)
Side effects	0	4 (6.8)

<sup>a</sup> Rates are for evaluable patients.

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TABLE 2. Susceptibility of *N. gonorrhoeae* (135 strains) to cefuroxime, penicillin, and ampicillin

Drug	MIC (mg/liter)		
	50%	90%	100%
Cefuroxime	0.015	0.06	0.25
Penicillin G	0.015	0.125	0.5
Ampicillin	0.25	0.5	1.0

In the cefuroxime group, 55 (96.5%) of the evaluable patients were cured, with 2 (3.5%) treatment failures at first test of cure. The six women and five homosexual men in this group were cured. There were only three patients (6%) with post-GC urethritis in the cefuroxime group. None of the patients receiving amoxicillin experienced any side effects, whereas four patients (6.8%) receiving cefuroxime had mild gastrointestinal side effects (nausea, mild diarrhea, and epigastric burning).

The MIC<sub>90</sub> (MIC for 90% of strains) was 0.06 mg/liter for cefuroxime, 0.125 mg/liter for penicillin G, and 0.5 mg/liter for ampicillin (Table 2). All strains were inhibited by 0.25 mg of cefuroxime per liter. Nine strains of  $\beta$ -lactamase-producing *N. gonorrhoeae* (obtained from other sources) were tested against cefuroxime, and all strains were inhibited by 0.25 mg/liter.

Amoxicillin (3.0 g) or ampicillin (3.5 g), with 1 g of probenecid, are the only single-dose oral regimens recommended by the Centers for Disease Control (1) for uncomplicated GC infections. Previous studies with oral ampicillin-probenecid combinations showed cure rates ranging from 90 to 100% (4, 6, 7, 10). Amoxicillin, which has an antibacterial spectrum similar to that of ampicillin, is better absorbed than ampicillin after oral administration; 3.0 g of oral amoxicillin is as effective as 3.5 g of ampicillin combined with 1 g of probenecid (5). The cure rate of 91.7% obtained in the amoxicillin-treated group is thus compatible with previous studies.

The cure rate of 96.5% obtained in the cefuroxime-treated group is not significantly different from the results in the amoxicillin-treated group ( $P > 0.1$ ), but approximately 350 patients would have to be studied to detect a 10% difference in response rate. It is unlikely, however, from the trends in this study that cefuroxime would prove significantly less effective than amoxicillin even with a larger study population. Previous studies showed that 1 to 1.5 g of parenteral cefuroxime with probenecid, administered intramuscularly, produced cure rates of 97 to 100% in males and females with GC infections (3, 9). Hence, the results with oral cefuroxime axetil are similar to those with the parenteral drug.

Although none of the patients in this study had  $\beta$ -lactamase-positive strains of *N. gonorrhoeae*, cefuroxime axetil may be useful in infections with these organisms because of its stability to the  $\beta$ -lactamase enzymes. It has been shown that 93% of GC strains are susceptible to 0.25 mg of cefuroxime per liter regardless of  $\beta$ -lactamase produc-

tion (12). No single-dose oral regimen is recommended by the Centers for Disease Control for  $\beta$ -lactamase-positive GC infections. However, recent studies have shown that norfloxacin (2), a quinolone derivative, and augmentin (13), amoxicillin combined with clavulanic acid, are effective single-dose oral regimens for infections caused by penicillin-resistant gonococci.

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