Comparison of Cefprozil and Cefaclor for Treatment of Acute Urinary Tract Infections in Women

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A total of 108 college women with acute urinary tract infections were treated for 10 days with either 500 mg of cefprozil (BMY-28100-03-800) once a day (n = 72) or 250 mg of cefaclor three times a day (n = 36). Clinical and bacterial cure rates at 1 week posttherapy were 94 and 93%, respectively, for the cefprozil group and 94 and 94%, respectively, for the cefaclor group (P, not significant). Both cefprozil and cefaclor were safe and effective.

Cefprozil (BMY-28100-03-800) is a new β-lactamase-stable oral cephalosporin, with broad in vitro activity against common urinary pathogens. Its activities are similar to those of cefaclor and greater than those of cephalaxin (5, 11, 17, 20, 24). Cefprozil is well absorbed from the gastrointestinal tract and is primarily excreted by the kidneys in active form (1-3, 22, 25). Its half-life (about 1.5 h) in plasma and plasma drug concentration-versus-time curve are twice those of cefaclor. Consequently, cefprozil attains levels in plasma above the MICs for susceptible organisms, lasting 2 to 8 h after dosing (1-3).

The pharmacokinetic profiles of cefprozil make it a desirable agent for once-a-day therapy of urinary tract infections. The objectives of this prospective, open study were to compare the safety and efficacy of a 10-day course of cefprozil (500 mg once daily) (BMY-28100-03-800; Bristol-Myers Squibb Co., Wallingford, Conn.) with the safety and efficacy of cefaclor (250 mg three times a day) (Ceclor; Eli Lilly & Co., Indianapolis, Ind.) and to assess the emergence of resistance in urogenital and bowel aerobic bacterial floras.

This trial was initially approved by our Institutional Review Board, and a signed, written consent form was obtained from each patient.

A total of 108 college women with symptoms of acute urinary tract infection were enrolled at the University of Florida Student Health Care Center UTI Clinic. To be included in the study, patients had to be females 18 years of age and older who had experienced (i) symptoms of dysuria, urgency, or suprapubic or loin pain, and (ii) bacteriuria confirmed by ≥10^5 CFU/ml of midstream clean-catch urine specimen. Patients were excluded if they were pregnant or lactating, had received antimicrobial agents during the preceding 2 weeks, or had impaired renal or liver function, urinary tract abnormalities, indwelling bladder catheter, or hypersensitivity to penicillin or cephalosporin.

Specimens were collected as previously reported (13). Urinary bacterial isolation and quantitative counts were performed as previously described (10, 16, 19, 26). Antibiotic susceptibility was tested with 30-μg cefprozil and cephalothin disks (4). Organisms were considered resistant if they had a zone of ≤12 mm for cefprozil and ≤14 mm for cephalothin. Coagulase-negative staphylococci were tested for novobiocin susceptibility with 5-μg disks (19). Swabs from vaginal, periurethral, and rectal sites were processed as previously reported (15).

Clinical evaluations and urine cultures were repeated within 3 to 5 days of initiation and at 5 to 9 days and 4 to 6 weeks posttherapy. During therapy, patients used diaries to record the times at which medication was taken and the times of resolution of symptoms. Clinical and bacteriologic responses were classified, as described previously (15).

Safety laboratory tests were performed prior to therapy, during days 3 to 5 of therapy, and 5 to 9 days posttherapy. Adverse events were monitored and recorded.

The life table method, the Fisher exact test, and chi-square analysis were used to compare treatment groups (6, 8, 23). The mean ages of patients in the cefprozil and cefaclor groups were 22 ± 4 and 22 ± 3 years, respectively. All patients had dysuria, frequency, urgency, and suprapubic pain. A total of 22% of the cefprozil patients and 25% of the cefaclor patients had costovertebral angle tenderness. The mean duration of symptoms before therapy was 4.8 ± 6 days in the cefprozil group and 4.3 ± 4 days in the cefaclor group. Of 109 pretherapy pathogens (one cefaclor patient had two pathogens), 108 (99%) were susceptible to cefprozil and 100 (92%) were susceptible to cephalothin (P = 0.024) (Table 1).

In vitro susceptibility results were also in agreement with those of previous reports (5, 11, 17, 20, 24). The mean duration of symptoms after the initiation of therapy was 49 ± 24 h in the cefprozil group and 50 ± 33 h in the cefaclor group (P, not significant).

Of 72 patients in the cefprozil group, 68 were clinically and bacteriologically evaluable. Of the four unevaluable patients, one received a concomitant antibiotic and three discontinued the drug because of adverse events. Of the 68 evaluable patients, 64 (94%) achieved clinical cures and 63 (93%) achieved bacteriologic cures at 5 to 9 days posttherapy. A total of 56 patients returned 4 to 6 weeks posttherapy. Three (4%) had relapses and three (4%) had reinfections. The cumulative rate of bacteriologic cure was 85%.

In the cefaclor group, 35 patients were clinically and bacteriologically evaluable. Of these, 33 (94%) achieved clinical and bacteriologic cures at 5 to 9 days posttherapy. A total of 33 patients returned 4 to 6 weeks posttherapy. The cumulative rate of bacteriologic cure was 91%, and one patient (3%) had a relapse (Table 2). There was no significant difference between the results of the two groups. These results were comparable to those of previous reports (7, 12, 15, 16, 18, 27).

Specimens were obtained from urogenital and rectal sites of 67 patients in the cefprozil group and 35 patients in the cefaclor group at pretherapy and 5 to 9 days posttherapy. Posttherapy, the frequency of Escherichia coli colonization...
of periurethral and vaginal sites decreased in both the cefprozil ($p = 0.003$ and $p = 0.001$, respectively) and the cefaclor ($p = 0.029$, and $p = 0.047$, respectively) groups. No significant change occurred in the frequency of $E. coli$ in the rectal flora posttherapy for either group. In the cefprozil group, the frequency of $E. coli$ resistant to cephalothin increased in the vaginal flora ($p = 0.044$) and the prevalence of cefprozil-resistant members of the family Enterobacteriaceae (other than $E. coli$) in the periurethral site ($p = 0.038$) and of cephalothin-resistant strains of the Enterobacteriaceae in the periurethral ($p = 0.005$) and vaginal ($p = 0.005$) sites increased, but there was no significant change in the prevalence of strains of the Enterobacteriaceae in the rectal flora. In the cefaclor group, no significant change occurred in the susceptibility patterns of $E. coli$ and of other members of the Enterobacteriaceae in these sites. The diverse effect of cefprozil versus cefaclor on the urogenital flora might be partly explained by the pharmacokinetic properties of these drugs. Cefaclor is absorbed (75 to 95%) rapidly from the intestine and excreted mainly in the urine within 2 h of oral dosing (2, 3, 25). Cefprozil is absorbed (66%) at a lower rate than cefaclor, allowing effective drug levels in plasma and urine for up to 8 h after oral dosing (1–3, 22, 25). It is likely that the longer exposure of the urogenital sites to the drug in the cefprozil group partly accounts for the more extensive changes in the frequency of bacterial colonization and bacterial susceptibility patterns. The effects of cefaclor on the urogenital and rectal flora described here are in agreement with previous reports (9, 15, 21).

Both drugs were well tolerated by 85 and 92% of the patients, respectively, ($p$, not significant). A total of 25 patients (35%) in the cefprozil group experienced at least one adverse event during therapy; of these, 3 (4%) had pruritic rash, 2 (3%) had nausea and vomiting, 2 (3%) had dizziness, and 1 (1%) had diarrhea. Three patients (4%) discontinued therapy, two because of nausea and vomiting and one because of a pruritic rash.

Nine patients (25%) in the cefaclor group reported at least one adverse event. Of these, two (6%) developed itching eyes (one with swollen eyelids) and one (3%) experienced vaginal spotting. Adverse events were mostly mild to moderate, transient, and consistent with those reported for cephalosporin (7, 12, 13, 15, 17, 18).

Candida vaginitis was experienced by 22% of the cefprozil and cefaclor patients at 5 to 9 days posttherapy, consistent with results reported for beta-lactam antibiotics (11). Posttherapy, 11% of the cefprozil patients had elevated transaminase enzymes. All blood chemistry remained normal in the cefaclor group. Leukopenia as low as 3,300 (normal range, 4,800 to 10,800) was reported for 14% of the cefprozil and cefaclor patients. Eosinophilia ranging from 5 to 19% (normal, 4%) was noted in 12% of the cefprozil and 8.3% of the cefaclor patients. All abnormal laboratory findings became normal by 2 weeks posttherapy. The reason for the higher incidence of abnormal laboratory tests in the cefprozil patients is not known. The small numbers of patients in the groups may, in part, explain this difference.

In conclusion, cefprozil and cefaclor are comparable for the treatment of urinary tract infections in women. The increased bacterial resistance in the urogenital sites and the greater frequency of abnormal safety laboratory tests in the cefprozil group warrant future studies with a larger group in order to determine their significance.

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## REFERENCES


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