Loracarbef versus Cefaclor in the Treatment of Urinary Tract Infections in Women

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In a double-blind, prospective, randomized study, 108 college women with acute urinary tract infections were treated for 7 days with either loracarbef (LY163892) at 200 mg once daily (n = 53) or cefaclor at 250 mg three times daily (n = 55). The cure rates at 5 to 9 days after treatment in the loracarbef and cefaclor groups were 96 and 90%, respectively. Both loracarbef and cefaclor are safe, well tolerated, and effective in the treatment of urinary tract infections in women.

Loracarbef (LY163892) is a new beta-lactam antibiotic with in vitro activity similar to those of cefaclor and amoxicillin-clavulanate potassium and superior to that of cephalaxin (4, 11, 19). Loracarbef is absorbed well from the bowel, attaining high levels above the MICs for susceptible organisms in plasma; it is excreted mostly in the urine in the active form. Loracarbef is resistant to plasmid-mediated ß-lactamases and has greater biochemical stability than cefaclor (3, 21, 22). These favorable characteristics make loracarbef a suitable antibiotic for once-a-day treatment of urinary tract infections (UTIs).

One purpose of this double-blind, randomized trial was to compare the safety and efficacy of a 7-day course of loracarbef (200 mg once daily) with cefaclor (250 mg three times a day) (Eli Lilly & Co., Indianapolis, Ind.) for treatment of acute UTIs. To maintain the blind study design, placebos were given to patients in the loracarbef group. A second purpose was to assess the emergence of resistant organisms in the genital and rectal aerobic flora. Prior to initiation, the trial was approved by our Institutional Review Board and signed written consent was obtained from each patient.

The patients studied were college women who came to the Kidney Clinic of the University of Florida Student Health Care Center. A criterion for inclusion was the presence of ≥10^5 CFU of the same bacterium per ml in each of two consecutive urine specimens. Excluded from the study were pregnant or lactating women; those with impaired renal or liver function, radiographically proven obstructive uropathy, or a history of allergy to penicillins or cephalosporins; and anyone receiving antimicrobial agents during the preceding week.

Two clean-catch midstream urine specimens were obtained within 48 h before treatment for analysis and culture. Specimens were collected from genitai and recta with Culturette rayon-tipped swabs (Scientific Products Div., Evanston, Ill.) for nonquantitative aerobic culture pretherapy and 5 to 9 days posttherapy.

Urinary bacterial isolation was performed and quantitative counts were determined as previously described (8, 16, 20, 26). Antibiotic susceptibility was tested by the disk diffusion method by using 30-µg disks of loracarbef and 30-µg disks of cephalothin (1). Bacterial isolates were considered susceptible to loracarbef or cefaclor when the disk zone sizes were ≥18 mm. Intermediate susceptibility was defined as <18 and ≥15 mm.

Swabs from vaginal, periurethral, and rectal sites were streaked onto MacConkey and blood agar plates. Each colony type was identified and scored on a three-point scale as follows: light (1+), 0 to 10 CFU; moderate (2+), 10 to 50 CFU; heavy (3+), >50 CFU. Susceptibility was tested as described above. Vaginal swabs were also tested for Candida albicans before and 5 to 9 days posttherapy as previously described (15, 16). Escherichia coli isolates were identified by serotype as previously reported (9, 23).

Clinical and bacteriological evaluations were repeated within 2 to 4 days of initiation of treatment and 5 to 9 days and 4 to 6 weeks posttherapy. During therapy, patients used diaries to record times of medication taking, voiding, and resolution of dysuria and urgency. Complete disappearance of symptoms by 5 to 9 days posttherapy was termed clinical cure, incomplete resolution was termed clinical improvement, and no apparent response was termed clinical failure. Bacteriologic responses were classified as short-term cures, long-term cures, failures, relapses, and reinfections, as described previously (15). The life table method and the chi-square and Fisher exact tests were used to analyze the data (5, 7).

Of 108 patients who entered the study (53 in the loracarbef group, 55 in cefaclor group), 104 (96.3%) were symptomatic, with a combination of dysuria, urgency, and suprapubic pain; 7 (15.7%) had costovertebral angle tenderness, and 1 had a fever of ≥38°C. There were no differences between the two groups with regard to pretherapy demographic findings and clinical presentation. In the loracarbef group, the mean age was 22.2 ± 4 years, symptoms were present 4.4 ± 4 days pretherapy. 17 patients (32.1%) had recurrent UTIs, and 51 (96.2%) had pyuria. In the cefaclor group, the mean age was

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>No. of isolates (no. resistant)</th>
<th>Loracarbef</th>
<th>Cefaclor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>36 (0)</td>
<td>38 (0)</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>4 (0)</td>
<td>4 (0)</td>
<td></td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>4 (0)</td>
<td>4 (0)</td>
<td></td>
</tr>
<tr>
<td>Enterobacter aerogenes</td>
<td>2 (2)</td>
<td>3 (2)</td>
<td></td>
</tr>
<tr>
<td>Citrobacter sp.</td>
<td>1 (0)</td>
<td>4 (0)</td>
<td></td>
</tr>
<tr>
<td>Nonhemolytic staphylococci</td>
<td>6 (1)</td>
<td>3 (1)</td>
<td></td>
</tr>
<tr>
<td>Enterococci</td>
<td>0 (0)</td>
<td>1 (0)</td>
<td></td>
</tr>
</tbody>
</table>

* Two patients in the cefaclor group each had two pathogens initially.
22.3 ± 3 years and symptoms were present 3.5 ± 12 days pretherapy. Fifteen patients (27.3%) had recurrent UTIs, and 55 (100%) had pyuria. The mean times until disappearance of symptoms after initiation of therapy were 48 (range, 4 to 234) h in the loracarbef group and 41 (range, 6 to 137) h in the cefaclor group. Four patients were asymptomatic. Distributions of urinary pathogens and their in vitro susceptibilities were comparable between groups (Table 1). Ninety-six percent of the urinary pathogens were susceptible to loracarbef, and 95% were susceptible to cefaclor. The 74 E. coli isolates were all susceptible to loracarbef and cefaclor. Four of five isolates of Enterobacter aerogenes were resistant to both agents. These results are in agreement with previous reports that loracarbef and cefaclor have comparable in vitro activities that are superior to that of cephalexin (2, 4, 11).

In the loracarbef group, 52 of 53 patients had sterile urine cultures after 2 to 4 days of therapy. One patient had a resistant pathogen pretherapy, and her urine culture remained positive. Her therapy was discontinued, as was that of three others, for the following reasons: one because of a low pretherapy bacterial count and two because of adverse reactions. In the cefaclor group, all 55 patients had sterile urine cultures after 2 to 4 days of therapy. Of the patients returning at 5 to 9 days posttherapy, 96% of the loracarbef group and 90% of the cefaclor group had short-term cures. Long-term cures occurred in 81% of the patients initially enrolled in each group who were available for long-term follow-up. Bacteriologic responses through 4 weeks posttherapy are shown in Table 2. Initially identified urinary pathogens remained eradicated at 4 to 6 weeks posttherapy in 37 (90%) and 39 (93%) of the patients in the loracarbef and cefaclor groups, respectively (P > 0.10). The therapeutic results of the two groups were favorable and comparable to those previously attained with antimicrobial agents, including cephalexin, in young women (6, 10, 12-14, 16-18).

Perirethral, vaginal, and rectal specimens were obtained from 46 patients in the loracarbef group and 51 patients in the cefaclor group. After therapy in both groups, the numbers of patients with cultures positive for colonizing E. coli in the perirethral (P < 0.001), vaginal (P < 0.001), and rectal (P < 0.01) flora were reduced. No significant change occurred in either (i) the number of patients with positive cultures for other members of the family Enterobacteriaceae or (ii) the susceptibility patterns of the bacteria colonizing these sites in either group. The findings related to cefaclor are in agreement with those previously reported (17, 18).

In the loracarbef group, five patients experienced adverse events: therapy was discontinued for two patients because of nausea, headache, and abdominal pain; two had nausea, one combined with a rash; and one experienced difficulty breathing and diarrhea on the last day of therapy. In the cefaclor group, three patients reported adverse events: two experienced diarrhea, one with nausea, and one developed a rash on the last day of therapy. Therapy was not interrupted for these three patients.

By 5 to 9 days posttherapy, Candida vaginitis developed in 8 (15.1%) of the patients in the loracarbef group and 11 (20.0%) of the patients in the cefaclor group. Laboratory test results did not significantly change for any patients in either group. These findings are consistent with those previously reported for cefaclor (13-15, 17, 18, 24, 25, 27, 28).

In conclusion, loracarbef and cefaclor are safe, well tolerated, and effective in the treatment of UTIs in women.

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REFERENCES

**TABLE 2. Distribution of patients by treatment group and bacteriologic response through 4 weeks after treatment ended**

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Who completed treatment and follow-up (5-9 days posttherapy)</th>
<th>With short-term:</th>
<th>Lost to follow-up after 5-9 days posttherapy</th>
<th>With long-term:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cure</td>
<td>Failure</td>
<td></td>
</tr>
<tr>
<td>Loracarbef</td>
<td>46</td>
<td>44 (96)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Cefaclor</td>
<td>51</td>
<td>46 (90)</td>
<td>5 (10)</td>
<td></td>
</tr>
</tbody>
</table>


