Single-Dose Cephalexin Therapy for Acute Bacterial Urinary Tract Infections and Acute Urethral Syndrome with Bladder Bacteriuria

J. CARDENAS, E. L. QUINN,* G. ROOKER, J. BAVINGER, AND D. POHLOD

Division of Fairlane and Division of Infectious Diseases, Department of Medicine, Henry Ford Hospital, Detroit, Michigan 48202

Received 20 May 1985/Accepted 29 November 1985

The efficacy of single-dose therapy with 3 g of cephalexin was evaluated in 129 women with symptoms of acute uncomplicated lower urinary tract infections. Of 91 patients with significant bacteriuria, 61 (67%) were cured of their original infection; this was similar to the 54 to 79% cure rates reported in unselected populations of women of a wide age range treated for acute uncomplicated urinary tract infections with a single dose of amoxicillin or trimethoprim-sulfamethoxazole (J. Rosenstock, L. P. Smith, M. Gurney, K. Lee, W. G. Weinberg, J. N. Longfield, W. B. Tauber, and W. W. Karney, Antimicrob. Agents Chemother. 27:652-654, 1985; N. E. Tolkoff-Rubin, M. E. Wilson, P. Zhuomskis, I. Jacoby, A. R. Martin, and R. H. Rubin, Antimicrob. Agents Chemother. 25:626-629, 1984). The cure rates of (87%) for our younger patients, those less than 25 years of age, was better than that (46%) for our patients over 40 years of age (P < 0.001). Patients with infections that were negative in an antibody-coated bacteria test were cured at a significantly higher rate than were those with infections that were positive in an antibody-coated bacteria test (71 versus 19%; P = 0.003). Those patients with infections caused by cephalexin-susceptible organisms were cured at a rate similar to that for patients with infections caused by cephalexin-resistant organisms (68 versus 50%; P = 0.62). The cure rate for suburban patients was 90%, versus 45% for inner-city patients (P = 0.008). Of the 28 women with acute urethral syndrome due to low-level bacteriuria, 27 were cured.

Urinary tract infections (UTI) affect at least 10% of the female population and are among the most common infections seen in general medical practice during a lifetime. In general, they are easy to diagnose and can be effectively treated with many different antimicrobial agents; however, the dosage and length of treatment are still controversial.

Recently, several studies showed that a single-dose regimen is effective in treating acute uncomplicated UTI in a selected population of women (12, 13). However, when unselected populations were studied, the single-dose regimen was less effective (6-8, 10, 11, 16).

Henry Ford Hospital is a 950-bed, outpatient, general medical facility in the inner-city area of Detroit with several satellite clinics in the suburbs. Observations of the patients in this institution gave us the opportunity to study different population groups living within the same large metropolitan area. We chose to investigate the efficacy of a single oral dose of cephalexin in treating acute uncomplicated UTI in women.

MATERIALS AND METHODS

Female patients who had symptoms suggestive of acute UTI (dysuria, frequency, hematuria) and had abnormal urinalysis results were entered in the study after informed consent was obtained. We excluded patients who were over 70 years of age, were pregnant, or showed evidence of hepatic or renal impairment or other concomitant infection. We also excluded patients who had signs of acute pyelonephritis, had recently used antibiotics, or had a history of cephalosporin hypersensitivity or complicated UTI (e.g., nephrolithiasis, indwelling catheter, etc.). Initially, 129 patients were entered in the study, but 4 were excluded from the final count because they were lost to follow-up. The remaining 125 patients were divided into three groups. Group 1 consisted of 91 patients whose pretreatment urine cultures yielded significant bacteriuria (≥50,000 CFU/ml); they were classified as having an acute uncomplicated UTI. Group 2 consisted of 28 patients whose pretreatment urine cultures contained ≤5,000 but <50,000 CFU of common uropathogens per ml; they were classified as having acute urethral syndrome due to bladder bacteriuria (14). Group 3 included six patients whose voided-urine cultures were sterile; they were classified as having nonbacterial acute urethral syndrome.

Patients received cephalexin in a single 3-g dose given as 3 1-g tablets in the presence of one of the investigators. Clean voided-urine specimens were obtained immediately before, 48 to 72 h after, and 7 to 14 days after treatment for urinalysis and culturing. Side effects were recorded at each clinic visit.

The antibody-coated bacteria (ACB) test was performed on the original urine specimens by the technique described by Thomas et al. (15). For the purpose of the present study, we required a positive test to show 4+ fluorescence with 100% of bacteria coated (J. Cardenas, D. Pohlod, and E. L. Quinn, Abstr. Annu. Meet. Am. Soc. Microbiol. 1983, A43, p. 8).

Outcome was considered satisfactory when symptoms and bacteriuria were resolved. Recurrence was defined as a reappearance of symptoms or a positive culture after a previously negative test. Recurrence with the same species was considered a relapse; recurrence was considered a reinfection if a new species of organism was cultured. Failure was defined as the persistence of symptoms or bacteriuria.

* Corresponding author.
TABLE 1. Outcome of single-dose treatment with cephalixin of patients with acute lower UTI due to significant bacteriuria in relation to age of patient, cephalixin resistance, and ACB test

<table>
<thead>
<tr>
<th>Age range</th>
<th>Patients cured/patients studied (%)</th>
<th>Cephalixin resistance (patients cured/patients studied)</th>
<th>Positive ACB test (patients cured/patients studied)</th>
</tr>
</thead>
<tbody>
<tr>
<td>19–24</td>
<td>21/24 (87)</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>25–29</td>
<td>14/18 (78)</td>
<td>0/1</td>
<td>0/1</td>
</tr>
<tr>
<td>30–34</td>
<td>7/12 (58)</td>
<td>1/1</td>
<td>0/1</td>
</tr>
<tr>
<td>35–40</td>
<td>8/13 (62)</td>
<td>1/2</td>
<td>0/1</td>
</tr>
<tr>
<td>40–70</td>
<td>11/24 (46)</td>
<td>1/2</td>
<td>0.3</td>
</tr>
</tbody>
</table>

* The average percentage of patients cured was 67. For age group 19 to 24 versus age group 40 to 70, P = 0.001 and chi-square test = 9.38.
* Of patients with cephalxin-resistant infections, 50% were cured.
* Of patients with a positive ACB test, 17% were cured.

RESULTS

The pathogen most commonly found was Escherichia coli (81%). Of the E. coli strains, 6% were resistant to cephalixin. Other isolates included Proteus mirabilis (7%), Staphylococcus saprophyticus (4%), Klebsiella pneumoniae (4%), and 1% each of Streptococcus group B, nonhemolytic streptococci, and Streptococcus group D. Of the patients, 2% had mixed infections.

Among the 91 patients with acute bacterial UTI (group 1), 87% (21 of 24) who were less than 25 years of age were cured (Table 1). In contrast, only 46% (11 of 24) of patients who were over 39 years of age (range, 40 to 75 years) were cured (P < 0.001). This difference was independent of a patient history of UTI (45 versus 33%, respectively). UTI in younger patients who were classified as a treatment failure or a recurrence were not due to cephalixin-resistant or antibody-coated bacteria. Only 1 of the 11 older patients had a UTI whose treatment was considered a failure; it was caused by a cephalixin-resistant strain. Three UTI in older patients were caused by antibiotic-coated bacteria. Treatment failure was thus related most closely to the age of the patient. In an analysis of age-related cure rates, Pauf et al. (7) reported cure rates of 85% for premenopausal versus 20% for postmenopausal women treated with a 1-day antimicrobial regimen.

The efficacy of single-dose therapy in the 91 patients of all ages in group 1 was 67%. Other investigators reported cure rates of 54 to 79% with single-dose therapy of acute uncomplicated UTI in an unsampled population of women (6,8, 10, 11, 16). In these studies, cure rates for specific age groups were not reported, and variables such as the duration of follow-up cultures were not uniform. Thus, a comparison of various studies was difficult. In all but one of the group 1 patients with positive cultures at 7 to 14 days UTI were caused by the same species of organism.

Only six of our patients had UTI caused by a cephalixin-resistant strain, and six had UTI associated with a positive ACB test (Table 1). Patients with UTI caused by cephalixin-susceptible organisms were cured at a rate similar to that for patients with UTI caused by cephalixin-resistant organisms (68 versus 50%; P = 0.62, chi-square test = 0.8). Patients with UTI that were negative in ACB were cured at a significantly higher rate than those with UTI that were positive in ACB test (71 versus 19%; P = 0.003, chi-square test = 9.2). The cure rate for patients living in the inner city was 45%, and that for patients living in the suburbs was 91% (P = 0.008, chi-square test = 12.4; Table 2). Greenberg et al. (4) and Rubin et al. (9) ascribed poor results in patients from the inner city to delay in seeking medical care. Furthermore, their inner-city patients often had upper urinary tract disease (3). Our inner-city patients had a higher rate of UTI that were positive by ACB test than did our suburban patients (22 versus 4%). However, treatment failures due to UTI that were negative in ACB test were also more frequent in the inner-city patients than in the suburban patients (33 versus 7%).

Of the 28 patients with acute urethral syndrome due to bladder bacteriuria (group 2), 27 achieved symptomatic and bacteriologic cure without recurrence.

Finally, of the six patients with initially sterile urine samples (group 3), one failed to achieve symptomatic relief from the single dose of cephalixin.

A total of 125 patients who received a 3-g dose of cephalixin were observed for drug-related side effects. Nine patients (6.4%) complained of gastrointestinal side effects consisting primarily of epigastric discomfort and nausea that lasted for less than 4 h. One patient had loose stools for 4 days, but the relation with the medication was not clear. An additional four patients (2.8%) developed vaginal moniliasis.

DISCUSSION

The clinical efficacy of cephalixin in treating UTI has been documented in numerous reports (3, 17). The use of a cephalosporin in a single dose for treating acute UTI was reported by Brumfitt et al. (1), who administered a single 2-g injection of cefaloridine; they reported a cure in only 16 of 25 women with UTI localized to the bladder. On the other hand, Greenberg et al. (4) reported that cefadroxil in a single 2-g oral dose cured 77% of UTI in patients with a negative ACB test. Multiple (250 mg three times daily) dosing for 10 days cured 80% of UTI in patients with a negative ACB test. However, the efficacy of single-dose therapy with cefadroxil was only 33% (10 of 30 patients) when results for all treated patients were analyzed.

The present study showed that the efficacy of cephalixin given as a single dose for acute uncomplicated UTI in 24 nonpregnant women aged 19 to 24 was 87%. None of the patients in this age group had cephalixin resistance or positive ACB test. Our results are not unexpected, considering the broad spectrum of antimicrobial activity of cephalixin as well as the high concentration achieved in the urine following an oral dose (5). However, the efficacy of cephalixin in the 91 patients of all ages was 67%. A review of published studies of single-dose treatment of acute uncomplicated UTI revealed very high cure rates (2, 13), but the drug regimens, type of population studied, and length of follow-up period differed notably in various studies, making a direct comparison difficult. More recently, an
efficacy of 54 to 79% was reported for unselected patients given single-dose treatment for acute uncomplicated lower UTI. McAllister et al. (6) reported that 72% (18 of 25) of women aged 18 to 55 years were cured when treated with a single 3-g dose of amoxicillin. Similar results were noted by Savard-Fenton et al. (10) for patients aged 16 years or older (mean, 31.2 years) who were treated with a similar single dose of amoxicillin; 66.6% (43 of 71) were cured. In the latter study, urine cultures were done 1 week after the completion of treatment. These authors concluded that single-dose treatment “with follow-up cultures” was a safe and effective treatment for nonpregnant women to ensure additional treatment for those who are not cured. In a report of a single-dose amoxicillin treatment by Rosenstock et al. (8) for women aged 15 to 82 years (mean, 44 years), only 54% (7 of 13) were reported cured when follow-up cultures were done at 14 and 28 days. These investigators noted that these results were lower than many reported in the literature, even if organisms resistant before treatment were excluded in the analysis of their cases. Pfau et al. (7), whose patients included both pre- and postmenopausal women given various antimicrobial agents in a 1-day treatment regimen, noted that the overall cure rate at 3 weeks follow-up was 74% (20 of 27). Schultz et al. (11) studied women aged 18 to 55 years who were given a single dose of trimethoprim-sulfamethoxazole. Relapse occurred in 10 of 68 women, and 15 women had a reinfection (overall efficacy rate, 63%). They believed that this empiric initial treatment of selected women with symptoms of acute uncomplicated UTI was practical, safe, and cost-effective. In a report of the use of a single dose of amoxicillin given to 210 women aged 18 to 65 years who had acute UTI, Tolkoff-Rubin et al. (16) noted that 165 (79%) women were cured of their original infection. They recommended initial single-dose therapy with follow-up cultures and a graded therapeutic approach. These reports and our findings suggest that if single-dose treatment is used, follow-up cultures are necessary to detect patients who need additional treatment. This is very important if one chooses to use single-dose therapy for patients living in the inner city and for older women.

The lack of ACB test standardization makes a comparison between studies difficult. We used very strict criteria to define a positive test (4+ fluorescence with 100% of bacteria coated) because we previously found that these criteria correlate best with the outcome of single-dose treatment (Cardenas et al., Abstr. Annu. Meet. Am. Soc. Microbiol. 1983). If we used parameters similar to those in other published reports (2+ fluorescence with >10% of bacteria coated), our overall results would not change significantly, but our success rate in treating ACB-positive patients would be 43% (6 of 14 cured) versus 17% (1 of 6 cured).

In our study, 28 patients had acute urethral syndrome due to bladder bacteriuria (14). Twenty-seven patients (96%) responded satisfactorily to the single cephalxin dose. These results, although not placebo controlled, suggest that most of the cases of acute urethral syndrome in the population were due to infections manifested by low bacterial colony counts with common uropathogens. Of further interest with regard to our patients was the close follow-up we were able to achieve for most patients because they belonged to a health maintenance organization and because their medical care was provided within our health care organization. No asymptomatic recurrences were seen in these successfully treated study patients during at least 1 year of follow-up.

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LITERATURE CITED