TREATMENT OF URINARY INFECTIONS IN PREGNANCY USING SINGLE VERSUS 10-DAY DOSING

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Pregnant patients with symptomatic and asymptomatic urinary tract infections were treated with a long and a short antibiotic regimen. Two hundred two patients were randomized prospectively to a single oral dose of 3.5 g ampicillin plus 1 g probenecid (98 patients) versus 500 mg ampicillin orally four times a day for 10 days (104 patients). The multiple-dose cure rate was statistically significantly better than that of the single-dose regimen (67.3% versus 57.1%, respectively). Interestingly, for resistant organisms, the cure rate for the long and short regimens was similar (48% versus 43%, respectively). In vitro susceptibility testing does not appear to be a good predictor of cure, at least for the single-dose group. Single-dose therapy with ampicillin and probenecid does not provide an optimal cure rate or prevent reinfection during pregnancy. Possible reasons for these findings are discussed. (*J Natl Med Assoc.* 1992;84:73-75.)

Key words • urinary tract infections • antibiotics • pregnancy

Urinary tract infections frequently complicate pregnancy. They may be symptomatic or asymptomatic and may involve the lower or upper urinary tract.

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Treatment regimens are often empiric. The antibiotic sensitivity of the offending organisms is usually known prior to treatment for patients with asymptomatic bacteriuria, but this information is not available when patients are treated for acute symptomatic disease.

Several authors have suggested that a standard 10-day course of antibiotic therapy may not be necessary for most cases of cystitis or asymptomatic bacteriuria. The results of shorter treatment courses in pregnant woman indicate cure rates between 47% and 93% for patients with antibiotic-sensitive isolates.[1-11] Variations in cure rates seem to depend on whether the upper tract is involved.[5]

This article reports the results of a prospective, randomized study that compared the efficacy of single-dose versus multiple-dose 10-day therapy in pregnant patients with both symptomatic and asymptomatic bacteriuria.

MATERIALS AND METHODS

Patients from the obstetric clinics at the Grady Memorial Hospital in Atlanta, Georgia were instructed in proper technique for clean-catch midstream urine collection. The urine samples were sent for culture and sensitivity. Candidates for the study were recruited from patients whose urine culture yielded a bacterial count greater than 10^5 colony forming units per milliliter (cfu/mL).

Patients with asymptomatic bacteriuria were included if the uropathogens isolated were sensitive to ampicillin. Patients with symptoms of cystitis were started on ampicillin after the sample collection, but before the culture results were available. Patients with symptoms of pyelonephritis or a history of penicillin allergy were excluded from the study.

Of 219 eligible patients, 202 completed the study. Study participants were assigned prospectively to one

TABLE 1. DISTRIBUTION OF PATIENTS WITH BACTERIURIA

	Group One	Group Two
Symptomatic	65	66
Asymptomatic	33	38
Total	**98**	**104**

TABLE 2. COMPARISON OF CURE RATES BETWEEN 1-DAY (GROUP ONE) AND 10-DAY (GROUP TWO) REGIMENS

Group	Cure Rate (%)
One	56/98 (57.1%)
Two	70/104 (67.3%)

of two treatment groups by pulling treatment indicator cards from shuffled sealed envelopes. Patients in group one were given a single oral dose of 3.5 g ampicillin plus 1 g of probenecid. Patients in group two were given 500 mg ampicillin capsules to be taken orally four times a day for 10 days.

Repeat urine cultures were obtained from all patients 2 weeks after therapy was started. Urine cultures were then repeated monthly until delivery. Positive cultures with the same organism at any time prior to delivery, ie, recurrences and relapses, were recorded as treatment failures.

Sixty-five patients in group one and 66 in group two had cystitis. Thirty-three patients in group one and 38 in group two had asymptomatic bacteriuria (Table 1).

Statistical evaluations were done using the chi square method.

RESULTS

There was a statistically significant difference in cure rates between the patients treated with the single-dose regimen and those treated with multiple doses over a 10-day period. Seventy patients (67.3%) in the multiple-dose group were cured compared with 56 (57.1%) in the single-dose group (Table 2).

Twenty-seven patients with cystitis in group two and 21 in group one had infections caused by ampicillin-resistant organisms. Thirteen patients (48%) with resistant organisms in group two and nine patients (43%) in group one were cured (Table 3).

Three patients (4%) in group one developed monilial vulvovaginitis compared with seven (9%) in group two.

TABLE 3. EFFECT OF THERAPY ON SYMPTOMATIC PATIENTS WITH LABORATORY EVIDENCE OF RESISTANT ORGANISMS

	No. With Resistant Organisms (%)	
Group	Resistant (%)	Cured (%)
One	21/65 (32.3%)	9/21 (43%)
Two	27/66 (40.9%)	13/27 (48%)

Three patients in group one and six patients in group two developed diarrhea.

The overall cure rate was superior for patients in group two, but complications were also more frequent.

DISCUSSION

The therapeutic goal for pregnant patients with urinary tract infections is cure and prevention of reinfection for the duration of the pregnancy. The efficacy of single-dose therapy is unacceptable for this goal. Patients with ampicillin-sensitive isolates were more likely to remain infection free with a 10-day regimen.

Our results suggest that in vitro susceptibility is not a good predictor of long-term cure for pregnant women with cystitis or asymptomatic bacteriuria. A single-dose regimen of 3.5 g of ampicillin plus 1 g of probenecid failed to cure or prevent relapse in 43% of patients with susceptible organisms. A 10-day course of 500 mg of ampicillin four times a day failed in 32.7% of cases. These results confirm the importance of obtaining frequent repeat urine cultures following treatment of urinary tract infections during pregnancy.

The reasons for increased susceptibility to infection and for reduced antibiotic effectiveness in pregnant women are conjectural. There may be an increased antibiotic distribution volume in pregnant women, an increased proportion of women with bacteriuria involving the upper tract, or even a better affinity of uropathogens to epithelial cells with the hormonal changes that occur in pregnancy.

Interestingly, 48% of patients with ampicillin-resistant bacteria were cured with the 3.5 g ampicillin and 1 g probenecid regimen, while 43% of patients with resistant strains were cured with the 10-day regimen. The cure rate for symptomatic patients with sensitive bacteria was not much better than the cure rate for patients with resistant organisms with the single-dose regimen. The cure rate for symptomatic patients with sensitive bacteria was significantly better than the cure rate for patients with resistant organisms with the 10-day regimen.

Reportedly, bacterial adherence is higher in patients who test positive for human leukocyte antigen A3 (HLA-A3) and for Lewis blood group nonsecretor phenotypes. It is possible that treatment failure with susceptible organisms occurs predominantly in patients with these or other similar predisposing factors.

Patients with bacteriuria of renal rather than bladder origin or patients with factors such as HLA-A3 or Lewis nonsecretor phenotypes may require more than single-dose therapy. If this is the case, single-dose therapy could be used to screen candidates for predisposing factors to infection such as HLA-A3, Lewis nonsecretor phenotypes, or upper tract disease.

It is possible that patients with asymptomatic bacteriuria of lower urinary tract origin may benefit from single-dose therapy if they are negative for HLA-A3 and Lewis nonsecretor phenotypes.

Whether the cure rate for pregnant women as defined in this study is improved with other antibiotics is yet to be determined. However, the advantages of single-dose therapy (eg, less fetal drug exposure, less side effects, and lower cost) justify further investigation into the factors that may be predictive of cure.

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