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3-Day Course of Ofloxacin versus Cefalexin in the Treatment of Urinary Tract Infections in Postmenopausal Women

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A short course of 200 mg of ofloxacin for 3 days was more effective and cheaper than a 7-day course of 500 mg of cefalexin four times a day in the treatment of postmenopausal women with urinary tract infections.

Cotrimoxazole and fluoroquinolones given as a short-course therapy, either as a single dose or for 3 days, have been cited as the optimal treatments for cystitis in young healthy women (1). In Israel, where more than 40% of the community uropathogens are resistant to cotrimoxazole, this drug cannot be used empirically (6). On the other hand, fluoroquinolones, despite their high efficacy, should not be considered the treatment of choice for uncomplicated cystitis, because they are expensive and because excessive use in the community could lead to the emergence of resistant strains. Beta-lactam agents represent a third category of antibiotics that are recommended for cystitis but only if administered for at least 5 days (5).

The optimal antibiotic and the duration of therapy for urinary tract infections (UTIs) in postmenopausal women are still matters of debate. Postmenopausal women, in contrast to younger women, have relatively high rates of failure or reinfection, and therefore UTIs in such patients may be considered complicated cystitis.

The aim of our study was to compare a short, 3-day course of the flouroquinolone ofloxacin with a conventional 7-day regimen of cefalexin in the treatment of cystitis in postmenopausal women.

Postmenopausal women who had been referred to our outpatient clinic with a diagnosis of lower UTI were included in the study. The diagnosis of lower UTI was based upon both clinical symptoms (dysuria, frequency of urination, and absence of fever or flank pain) and laboratory findings (pyruia [at least eight leukocytes per mm^3] and a positive urinary culture yielding $\geq 10^5$ CFU/ml). Exclusion criteria were as follows: serum creatinine concentration of >1.8 mg%, a neurogenic bladder, nephrolithiasis, or a permanent indwelling urinary catheter, diabetes or any other immunosuppressive disease, cystoceles grade II-III, and the presence of urinary pathogens resistant to one of the agents used in the study.

Clean, voided, midstream urine samples were collected and cultured by the Uritest system (Hylab dip slides; Hylab, Rehovot, Israel). All isolates were identified by standard procedures and tested for susceptibility to antimicrobial drugs by the Kirby-Bauer method.

Treatment was assigned by using a randomized open design. One group received 200 mg of ofloxacin once daily for 3 days, and the second group received 0.5 g of cefalexin four times a day for 7 days. The women were asked to return 3 to 5 days after treatment (short-term follow-up) and 28 days after treatment (long-term follow-up). At each visit, the patients were asked about urinary symptoms and adverse events, and a midstream urine sample was collected for culture.

In this study, bacteriological cure was defined as eradication of the causative organism (sterile culture at short-term follow-up), persistence (presence of the causative organism), or superinfection (a new pathogen present in the urinary culture). Bacteriological response at the 4-week follow-up was defined as continued eradication or eradication with relapse or reinfection. Clinical response was based on the assessment of signs and symptoms present at the initial visit on admission. At the short-term follow-up, the clinical response was defined as resolution (disappearance of all signs or symptoms), improvement, or failure (persistence of complaints). At 4 weeks, the clinical response was defined as continued resolution or symptom renewal. A positive culture without clinical symptoms was defined as asymptomatic bacteriuria.

Adverse events were recorded and classified as mild, moderate, severe, or life-threatening.

Statistical analysis was performed by the chi-square test with Yates' correction where appropriate, and P values of 0.05 were considered statistically significant. The size of the study group was set so that a clinically significant difference of 20% or more between treatment groups, with a two-sided type I error (α) of 0.05 and a type II error (β) of 0.2, could be detected.

Of the 250 enrolled women, 223 were evaluable for treatment outcome; 119 received ofloxacin, and 104 received cefalexin. Women dropped out of the study for the following reasons: a total of nine women because of a negative pretreatment culture, four from the ofloxacin-treated group and five from the cefalexin-treated group; five and six because of a violation of the protocol; and two and five because of nonconclusion of the follow-up, respectively.

The mean age of the ofloxacin-treated women was 65.4 ± 18.2 years, and the mean age of the cefalexin patients was 66.1 ± 20.1 years. Recurrent UTIs (three or more episodes of UTI in the last year or two or more episodes during the last 6 months) were found in 100 and 95 women, respectively. At the first follow-up, 3 to 5 days after cessation of therapy, 92 of 119 (77.3%) women who received ofloxacin had sterile urine, in contrast to 66 of 104 (63.5%) in the cefalexin group ($P = 0.02$). At day 28, 88 (73.9%) ofloxacin patients and 63 (60.5%) cefalexin-treated patients remained free of bacteria ($P = 0.02$). Persistent infection was present in 17 ofloxacin patients (14.2%) and 36 cefalexin patients (34.6%) ($P < 0.001$). The clinical responses were similar in the two groups (Table 1). At the short-term follow-up, 77% of patients in both groups showed a resolution of symptoms. However, at the long-term follow-up, 90 of 92 ofloxacin patients remained symptom-free,

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TABLE 1. Microbiological and clinical responses

Response	No. of patients with response (%)		*P* value[a]
	Ofloxacin group (n = 119)	Cefalexin group (n = 104)	
Microbiological			
3–5 days after therapy			
Eradication	92 (77.3)	66 (63.5)	0.02
Persistence	17 (14.3)	36 (34.6)	<0.001
Superinfection	10 (8.4)	2 (1.9)	
28 days after therapy			
Continued eradication	88 (73.9)	63 (60.6)	0.03
Eradication with relapse	2 (1.7)	1 (0.9)	
Eradication with reinfection	2 (1.7)	2 (1.9)	
Clinical			
3–5 days after therapy			
Resolution	92 (77.3)	80 (76.9)	0.9
Failure	27 (22.7)	24 (23.1)	
28 days after therapy			
Continued resolution	90 (75.6)	70 (67.3)	0.008
Symptom renewal	2 (2.5)	10 (9.6)	

[a] *P* value for the two values found for the ofloxacin and cefalexin groups.

whereas only 70 of the 80 cefalexin patients continued to have no symptoms (P = 0.008). Table 2 shows the microorganisms which were successfully eradicated by the antibiotics at short-term follow-up.

Adverse events occurred in five women in each group, but these events were mild and did not require cessation of treatment. These adverse events were gastrointestinal complaints in two and three women, dizziness/headache and pruritis in two and one ofloxacin-treated patients, and *Candida* vaginitis in two women who received cefalexin.

The cost of the 3-day ofloxacin treatment was $4.8, whereas the cost for the 7-day cefalexin treatment was $6.8.

This is the first study to evaluate a short-course antibiotic therapy for UTI specifically in postmenopausal women. Our study population included patients with a prior high risk of failure or relapse, since these women were elderly (mean age, 65 years old) and 87% of them had a history of recurrent UTI. Nevertheless, a short-course 3-day regimen of 200 mg of ofloxacin once a day achieved significantly better microbiological rates of eradication than the conventional 7-day treatment of 500 mg cefalexin four times a day (77.3% versus 63.5% [P = 0.02]). The better microbiological response obtained with ofloxacin persisted for 28 days. It has been suggested that quinolones such as ofloxacin are highly effective in treating UTI because of their ability to reduce the number of *Escherichia coli* in the rectum and vagina, in contrast to beta-lactam agents, which have little effect on vaginal and rectal flora (3). In a previous study by Hooton et al. (2), ofloxacin (200 mg twice a day) administered for 3 days was associated with a 96% microbiological cure rate, which is a higher cure rate than the rate we found. This difference may be due to the different dosage schedule used (twice daily versus once daily). Moreover, Hooton's study population consisted of young women, and only 31% of them had a history of recurrent UTIs in contrast to 87% in our study. Iravani et al. (4) also evaluated three treatment regimens for UTI using two different quinolones in women ≥40 years old. The eradication rates with ciprofloxacin (0.5 g once a day) administered for 3 and 5 days were 75 and 63%, respectively. A 7-day course of 400 mg of norfloxacin twice a day was more effective, leading to a 93% eradication rate. Thus, the 75% microbiological cure rate for the 3-day ciprofloxacin therapy was quite similar to the 77% cure rate we obtained with ofloxacin. It is possible that we too would have achieved even higher rates (approaching 90%) had we included a third group receiving ofloxacin for 7 days or alternatively administered 400 mg of ofloxacin daily instead of 200 mg daily.

TABLE 2. Microorganisms eradicated by ofloxacin and cefalexin at short-term follow-up

Microorganism	No. of patients showing eradication/total no. of patients (%)	
	Ofloxacin group (n = 92)	Cefalexin group (n = 66)
Escherichia coli	86/104 (82.7)	62/86 (72.0)
Klebsiella pneumoniae	3/7 (42.8)	1/12 (8.3)
Proteus mirabilis	2/6 (0.3)	1/3 (1.3)
Morganella morganii	1/2 (0.5)	2/3 (0.6)

The new fluoroquinolones are generally considered to be too costly for treating a very common, relatively benign disease. In this study, however, a 3-day course of low-dose ofloxacin was $2.00 cheaper than the standard 7-day cefalexin regimen.

In Israel, where the empiric use of cotrimoxazole for UTI is not appropriate, short-course therapy with low-dose ofloxacin is an attractive option. However, despite superior efficacy, low cost, and high patient compliance, we believe it is premature to recommend the use of fluoroquinolones as a first-line treatment for cystitis in elderly women.

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REFERENCES

1. **Counts, G. W., W. E. Stamm, M. McKevitt, K. Running, K. K. Homes, and M. Turck.** 1982. Treatment of cystitis in women with a single dose of trimethoprim-sulfamethoxazole. Rev. Infect. Dis. **4:**484–490.
2. **Hooton, T. M., R. H. Latham, E. S. Wong, C. Johnson, P. L. Roberts, and W. E. Stamm.** 1989. Ofloxacin versus trimethoprim-sulfamethoxazole for treatment of acute cystitis. Antimicrob. Agents Chemother. **33:**1308–1312.
3. **Hooton, T. M., C. Winter, F. Tiu, and W. E. Stamm.** 1995. Randomized comparative trial and cost analysis for three day antimicrobial regimens for treatment of acute cystitis in women. JAMA **273:**41–45.
4. **Iravani, A., A. D. Tice, J. McCarty, et al.** 1995. Short-course ciprofloxacin treatment of acute uncomplicated urinary tract infection in women. The minimum effective dose. Arch. Intern. Med. **155:**485–494.
5. **Noorby, S. R.** 1990. Short-term treatment of uncomplicated lower urinary tract infections in women. Rev. Infect. Dis. **12:**458–467.
6. **Raz, R., H. Hefter, B. Oren, Y. Keness, and Y. Potasman.** 1993. Antimicrobial resistance of urinary isolate in the community and its relation to antibiotic use. Isr. J. Med. Sci. **29:**207–210.