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ORIGINAL PAPER

Evaluation of Efficacy of Fosfomycin for the Treatment of Patients with Lower Urinary Tract Infections (UTIs)

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ABSTRACT

Introduction: *Until now, there have been few investigations on the efficacy of fosfomycin in the treatment of patients with uncomplicated urinary tract infections (UTIs). The present study is aimed to examine how fosfomycin affects females with lower UTIs.*

Methods: *A total of 200 female patients who visited the women's clinic at Amir-Al-Momenin Hospital between 2020 and 2021 were examined in the present study. Patients were randomly divided into two groups of 100 people each, with one group receiving fosfomycin (a single 3 g dose) and the other one receiving cephalexin (a five-day regimen at 0.5 g four times daily). Then, one week and one month after treatment, the patients underwent a urine culture test. The data were collected and further analyzed in SPSS statistics software version 26.*

Results: *According to the study findings, the mean age of females suffering from lower UTI was 25.45 ± 5.85 years. Besides, the collected data revealed that 85.5% of females diagnosed with lower UTI had* E. coli. *In addition, the frequency of females with* Staphylococcus saprophyticus, Proteus *spp and* Klebsiella *were 9%, 3% and 2.5%, respectively. Also, the frequency of women with UTI for* E. coli, Staphylococcus saprophyticus, Proteus *spp and* Klebsiella *were 85.5%, 9%, 3.2% and 2.5%, respectively. One month after treatment, urine culture showed positive results in 98% of patients who were treated with fosfomycin and 95% of those who received cephalexin.*

Conclusion: *Fosfomycin can be administrated to treat uncomplicated UTIs in women with a high level of confidence, as an alternative to cephalexin.*

Keywords: lower urinary tract infection (UTI), fosfomycin, cephalexin.

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INTRODUCTION

The urinary tract is one of the organs that is affected by infectious agents in various ways. UTI is considered a syndrome, similar to other ones, with multiple factors contributing to its occurrence (1). Lower UTI is a term used to describe the inflammation caused by microbial mismanagement. It is a prevalent condition among women referring to public health services. Approximately 2–5% of women who have consulted with healthcare providers have presented symptoms of UTI infection (2-4). Recurrent urinary tract infections (RUTI) are a major concern among women. The findings suggest that RUTI may occur twice or more often in 20-30% of women with UTIs, while 5% may develop chronic UTI (5).

Frequently encountered masses causing UTIs in women of this age group are *E. coli*, *Staphylococcus saprophyticus*, *Klebsiella* and *Proteus*. Anyway, urine culture samples reveal that *E. coli* is responsible for 80% of cases by itself. The diagnosis of UTI in women is primarily based on clinical examination and treatment typically begins with common masses, notably *E. coli*. The confirmation of clinical diagnosis was done using complete urine examination test and urine culture (4). Fosfomycin has been introduced by the European Urology Association (EAU) to treat urinary tract infections.

Fosfomycin is an antibiotic used to treat bladder infections such as acute cystitis or lower urinary tract infection in women, which works by stopping the growth of bacteria. It is therefore used to treat bacterial infections and has no effect on viral infections. Fosfomycin is an antibiotic that effectively acts on the biosynthesis of bacterial peptidoglycan. It hinders the production of N-acetylmuramic acid, which is one of the initial stages of peptidoglycan synthesis, thereby preventing the formation of peptidoglycan. Moreover, fosfomycin increases the susceptibility of bacteria to osmotic and lysosomal pressure under normal conditions. Fosfomycin is a commonly prescribed antibiotic that prevents *Staphylococcus aureus* infections and is also sensitive to methicillin. On the other hand, the concurrent administration of fosfomycin with other antibiotics can enhance their effectiveness (6, 7). To date, some studies have reported the efficacy of administering fosfomycin in the treatment of patients with uncomplicated lower UTIs. Although a limited number of studies have been conducted so far, the available research has indicated minimal side effects associated with the administration of fosfomycin. Consequently, the present study is a randomized clinical trial which aims to evaluate the effectiveness of oral fosfomycin in treating lower UTI. ❑

METHODS

This is one of the interventional studies and clinical trials conducted between 2020 and 2021 on female patients with lower UTI who were referred to the women's clinics of Amir-Al-Momenin Hospital. If we take the α (type I error) as 0.05, the d (accuracy) as 0.1, and the p as 0.5, the equation suggests that the study should include 200 individuals.

$$n = \frac{p(1-p) * Z^2_{1-\alpha/2}}{d^2} = 200$$

Convenience sampling was the sampling strategy used in the present study. The study involved the examination of 200 female patients who visited the women's clinic at Amir-Al-Momenin Hospital between 2020 and 2021. Patients were randomly divided into two groups of 100 people each, with one group receiving fosfomycin and the other one receiving cephalexin. Then, one week and one month after treatment, patients underwent a urine culture test. Patients who met the inclusion criteria and had a positive culture upon visiting the clinic were treated with a single 3 g dose of fosfomycin and a five-day regimen of cephalexin at 0.5 g four times daily (8). One week and one month after treatment, a urine culture test was done in all patients. The data was collected and then analyzed using SPSS software, version 26.

The individuals who entered the study were only unmarried females between the ages of 13 and 25 years old who had experienced symptoms for less than seven days and had a positive culture during their initial visit. The symptoms that were taken into account included frequent urination, overactive bladder, burning urine, and abdominal pain, and the patient had to have at least two of these symptoms. On the other hand, the exclusion criteria comprised patients with complicated

UTIs, pregnant women, male patients, individuals with chronic underlying and incurable diseases such as blood diseases, liver disease, or diabetes, patients who had received antibiotics within the last three weeks, or those who had received or were compelled to use another drug concomitantly. Acutely unwell patients and those with fever, patients with drug sensitivity to fosfomycin, and those who have had UTIs more than three times during the year were also excluded from the study.

Data analysis

The statistical analysis of all data was performed using SPSS version 26 software. For quantitative variables, the mean and standard deviation were measured, while absolute and relative frequency were calculated for qualitative variables. In order to examine the research hypotheses, the Chi-square test was employed with a significance level of 0.05.

Ethical considerations

None of the participants in this study were compelled to partake in the research. To adhere to ethical principles, the study procedure was explained to the participants prior to commencement, and their voluntary consent was obtained prior to their inclusion in the study. ❑

RESULTS

The study comprised 200 female patients diagnosed with lower UTI who had positive urine cultures and were referred to the women's clinics at Amir-Al-Momenin Hospital between 2020-2021. According to the findings summarized in Table 1, the mean age of female participants with lower UTI was 25.45 ± 5.85 years, with 51% falling within the 25-35 age bracket.

According to the data presented in Table 2, most women (85.5%) had UTI with *E. coli*. Additionally, 9% of the women had *Streptococcus saprophyticus*, 3% had *Proteus* and 2.5% *Klebsiella*.

TABLE 1. Age distribution of female patients with UTI referred to women's clinics of Amir-Al-Momenin Hospital

Age (years)	Frequency	Percentage
Under 25	6	3
25-35	102	51
35-45	68	34
Over 45	24	12
Standard deviation ± mean	25.45 ± 5.85	

Result of urine culture test	Frequency	Percentage
E. coli	171	85.5
Streptococcus saprophyticus	18	9
Proteus	6	3
Klebsiella	5	2.5

TABLE 2. Frequency of the first urine culture test based on the microbe type

Clinical symptoms	Frequency	Percentage
Dysuria	176	88
Urinary retention	159	79.5
Frequent urination	181	90.5
Fever	49	24.5

TABLE 3. Frequency of clinical symptoms of patients with lower UTI

TABLE 4. Results of urine culture test one week after treatment in the studied groups

Group	Result of test	Frequency	Percentage	Chi-square	P-value
Fosfomycin	Negative	92	92	8.34	0.047
	Positive	8	8		
Cephalexin	Negative	89	89		
	Positive	11	11		

TABLE 5. The results of urine culture test one month after treatment in the studied groups

Group	Result of test	Frequency	Percentage	Chi-square	P-value
Fosfomycin	Negative	98	98	6.34	0.056
	Positive	2	2		
Cephalexin	Negative	95	95		
	Positive	5	5		

The clinical symptoms of patients with lower UTIs are shown in Table 3. The findings indicate that the prevailing clinical symptoms were frequent urination, experienced by 90.5% of patients, dysuria by 88%, urinary retention by 79.5% and fever by 24.5% of subjects.

According to the data presented in Table 4, after one week of treatment, a positive result of the urine culture test was observed in 8% of patients who received fosfomycin and 11% of those who were given cephalexin. The results of the Chi-square test indicate that there is a significant effect of fosfomycin after one week of treatment (P-value <0.05).

After one month of treatment, the urine culture test showed a positive result in only 2% of patients who received fosfomycin, whereas in those treated with cephalexin, the rate of positive cases was 95%. As demonstrated in Table 5 and in accordance with the results from the Chi-square

test, there is no significant difference between the effectiveness of fosfomycin and cephalexin one month after the treatment of lower UTI (P-value >0.05). ❑

DISCUSSION

To date, there have been only a few studies that have focused on the efficacy of treatment with fosfomycin trometamol in patients with uncomplicated lower UTI. Consequently, this clinical trial aimed to investigate the efficacy of fosfomycin trometamol in treating lower UTIs. In this regard, a total of 200 patients with lower UTI, with a mean age of 25.45 ± 5.85 years, were enrolled in the present study. Also, 51% of participants belonged to the age group of 25-35 years. Baerheim *et al* (1994) reported a higher incidence of lower UTIs in the age group of 20 to 30 years, which was consistent with our findings (9). According to the study by Sheffield *et al*, the mean age of patients with lower UTIs was 26 years, which was in line with the findings of the present study (10). Since lower UTIs are more prevalent in individuals under 40 compared to other age groups, conducting a study to identify the risk factors associated with UTIs can yield valuable insights.

The study found that among women with lower UTIs, 85.5% had *E. coli*, 9% *Streptococcus saprophyticus*, 3% *Proteus* and 2.5% *Klebsiella*, which was consistent with the findings reported by the study of Karimi *et al* in 2012 (11). Foxman *et al* (2010) found that the most prevalent type of infection was associated with E. coli (12), which was consistent with our findings. Dwyer *et al* (2002) reported that 11% of patients with lower UTI were infected with *Streptococcus saprophyticus* (13), which was in line with our study results. Based on the findings of the present study, the most prevalent clinical symptoms were frequent urination, experienced by 90.5% of patients, dysuria by 88%, urinary retention by 79.5% and fever by 24.5% of patients. Davis *et al* (2017) reported that frequent urination was the most prevalent symptom of UTI (14), which was in line with the findings of the present study. Baerheim *et al* (1992) found that dysuria was the most prevalent symptom of UTI (15), which was more frequent compared with the present study.

After a week of treatment, 92% of patients who received fosfomycin exhibited negative results in their urine culture test. Karimi *et al* found that the success rate of fosfomycin treatment after one week was 91.7%, which was in line with our findings (11). According to the results of a study by Elhanan *et al* (1994), the success rate of fosfomycin treatment was 83%, which (8) was lower than that found by us. Based on the data reported by Krcmery *et al* (2001), a success rate of 95.2% was reported in treating patients one week after administering fosfomycin, which was higher than the data provided by the present study (16). According to the study conducted by Bayrak *et al* (2007), the effectiveness rate of fosfomycin was reported to be 93.5%, which was in line with our findings (17). Stein *et al* (1999) found that fosfomycin had a greater therapeutic success compared to cephalexin after one week of treatment, which was in line with the findings of the present study (18).

After a month of treatment, 98% of patients who received fosfomycin showed successful results in their urine culture test. According to the study by Minassian *et al* (1998), there was a therapeutic success rate of 97% one month following the administration of fosfomycin, which was in line with the findings of the current study (19). Karimi *et al* (2012) found that there was no significant difference in the long-term treatment of lower urinary tract infection between fosfomycin and cephalexin, which was consistent with the findings of the present study (11). However, there was no significant difference between the administration of fosfomycin and cephalexin in the treatment of lower UTI in the long term, which was consistent with the findings of Karimi *et al* (11). According to the results of similar studies in the past and those reported by us in the current research, it can be said that fosfomycin is effective in the treatment of UTIs in women (8-22).

A noteworthy aspect of the present study is that it is the first internal investigation to examine the effectiveness of fosfomycin in treating lower UTIs. Our study had certain limitations such as the inability to examine the side effects of fosfomycin among patients. However, the availability of such information could provide valuable insights and aid in making more accurate decisions in future research. ❑

CONCLUSION

The findings of the present study revealed that the use of fosfomycin resulted in the succes-

sful treatment of lower UTI in 92% of patients within the first week and in 98% of patients after one month of use. Given that there was no significant difference in the effectiveness of fosfomycin and cephalexin, and the convenience of a single dose of fosfomycin, which was more acceptable to patients, we concluded that fosfomycin could serve as a substitute for cephalexin. Fosfomycin has proven efficacy in treating uncomplicated UTIs in women and can be confidently used for this purpose. ❑

Conflicts of interest: none declared.
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