

STUDY OF FOSFOMYCIN TROMETAMOL IN ACUTE LOWER URINARY TRACT INFECTIONS

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ABSTRACT

OBJECTIVES

To evaluate the efficacy of single oral dose of Fosfomycin Trometamol (FT) in patients of uncomplicated lower urinary tract infections.

METHODS

One hundred women between 18-65 years' age group with uncomplicated Urinary Tract Infection (UTI) with culture positive for *E. coli* and *Enterococcus* were enrolled in this prospective study. Patients with culture positive for *E. coli* and *Enterococcus* and with in-vitro susceptibility to Fosfomycin Trometamol (FT) as tested by Kirby-Bauer disc diffusion method were given single oral dose of Fosfomycin trometamol, i.e. 3 g. These patients were followed up for clinical and bacteriological cure and any adverse effects.

RESULTS

The incidence of *E. coli* infection was 86% and *Enterococcus* infection was 14%; 78% of *E. coli* isolates were susceptible to FT with 22% being resistant; 86% of *Enterococcus* isolates were susceptible to FT with 14% being resistant. Incidence of adverse effects of FT was only 2%.

CONCLUSIONS

Fosfomycin trometamol might be considered as a promising single dose oral antibiotic for uncomplicated UTI due to *E. coli* and *Enterococcus* spp.

KEYWORDS

Urinary Tract Infections, Fosfomycin Trometamol, *E. coli*, *Enterococcus*, Adverse Effects.

HOW TO CITE THIS ARTICLE: Bedi P, Singh K, Wariach P. Study of fosfomycin trometamol in acute lower urinary tract infections. *J. Evolution Med. Dent. Sci.* 2016;5(31):1649-1650, DOI: 10.14260/jemds/2016/388

INTRODUCTION

Urinary tract infection is the second most common bacterial infection after respiratory tract infection. These infections occur more frequently in female population, almost four times than males with 60% of women having at least one infection at some point in their lives. They occur most frequently in sexually active females with 10% of women getting infection every year. Recurrences are common with nearly half of people getting a second infection within a year, either with different organism or reinfection with the same organism. Risk factors include female anatomy, sexual intercourse, family history or it may also result from blood borne infection. Uncomplicated UTI is defined as an infection occurring in a structurally and functionally normal urinary tract. Complicated UTI refers to infection in a urinary tract with abnormalities. The pathogenesis of UTI depends on the results of an interaction between bacterial virulence and host defence mechanism.

Although UTIs are caused by many micro-organisms, the most frequent aetiological agent is *E. coli* (80% of cases).¹

Financial or Other, Competing Interest: None.

Submission 29-02-2016, Peer Review 24-03-2016,

Acceptance 30-03-2016, Published 18-04-2016.

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DOI: 10.14260/jemds/2016/388

Uncomplicated infections can be diagnosed and treated based on symptoms alone. Oral antibiotics such as trimethoprim/sulfamethoxazole, nitrofurantoin or fosfomycin are typically first line antibiotics. Extended-spectrum Beta Lactamase (ESBL) produced by *E. coli* limits the treatment options. FT is a preferred broad-spectrum phosphoenolpyruvate analog antimicrobial agent in uncomplicated lower UTIs due to advantage of single dose use, rare side effects and low resistance rates.²

MATERIALS AND METHODS

This prospective study was conducted in the Department of Obstetrics and Gynaecology, Bebe Nanaki Hospital and Department of Microbiology, Govt. Medical College, Amritsar. Patients in age group of 18-65 years with complaints of dysuria, urgency, frequency, pain lower abdomen, fever, etc. were subjected to detailed history, clinical examination, urine microscopic examination and urine for culture sensitivity. Patients with structural abnormalities of urinary tract, complicating factors like diabetes mellitus, obstructive uropathy like ureteric stones were not included in the study. One hundred patients were selected with urine culture positive for *E. coli* and *Enterococcus*.

Midstream clean catch urine samples from patients were collected in sterile containers and transported to microbiology laboratory.

Isolation and identification of isolates from urine specimen was carried out by using a semi-quantitative culture method as per standard protocol.

Antimicrobial-susceptibility testing was carried out using the Kirby-Bauer disc diffusion technique; 200 µg fosfomycin (With 50 µg glucose-6-phosphate) discs were used. The diameter of the zones of inhibition for fosfomycin were interpreted according to the CLSI guidelines [Susceptible (≥ 16 mm), intermediate (13-15 mm) or resistant (≤ 12 mm)].

The patients susceptible to FT on urine for culture sensitivity test were given single oral dose of 3 g of FT stat. These patients were subjected to repeat urine culture sensitivity after 48 hours of drug intake. The results were tabulated and evaluated to find the efficacy of FT single dose in improving the clinical and bacteriological results.

RESULTS

In the present study, 78 out of 100 (78%) patients were in age group of 18-30 years and 20% of the patients belonged to age group of 31-45 years; 46-65 years of age group was represented by only 2% of patients. Out of 100 patients, 86% of the patients were found to be infected with *E. coli* and 14% of the patients were infected with Enterococci as per their urine for culture sensitivity report.

Out of 86 *E. coli* isolates, only 67 (78%) were susceptible to FT and 19 (22%) were resistant. Out of 14 Enterococcus isolates, 12 (86%) were sensitive to FT and 2 (14%) were resistant. The resistance to FT seems to be either chromosomally or plasmid mediated. The chromosomal mutations act by altering the intracellular transport mechanisms of fosfomycin. Fosfomycin may also become inactive because of mutations, which make its target enzyme (Pyruvyl transferase) unable to distinguish between the substrate (Phosphoenolpyruvic acid) and fosfomycin.

Out of 79 patients who were treated with 3 gm single oral dose of FT, none of the patients showed persistence of infectious agent in the urine as evidenced by no growth of the offending organism in the repeat urine for culture sensitivity test.

Only 2% of the patients who were treated with FT showed adverse drug effects in the form of nausea and epigastric discomfort.

DISCUSSION

Uncomplicated urinary tract infection is an infection occurring in a structurally and functionally normal urinary tract. *E. coli* and Enterococcus spp. together account for more than 80% cases of uncomplicated UTIs. Sahni et al. and Mengelloglu et al. found the incidence of *E. coli* infection to be 77% and 78% respectively with incidence of Enterococcus to be around 9%.^{3,4} 7-10 days of antibiotic therapy is routinely recommended for such patients. However, it has become apparent that most women have only a superficial mucosal infection and can be cured with much shorter courses of therapy. Fosfomycin trometamol is a phosphonic acid derivative, which acts by inhibiting biosynthesis of peptidoglycans required for bacterial cell wall synthesis. It is given as a single oral dose of 3 g.

In the present study, the efficacy of fosfomycin trometamol as a single dose oral treatment for achieving bacteriological cure ranged from 80-90%. Raz et al. also found that FT was the most active antibiotic agent against *E. coli* and Enterococcus spp. with an overall susceptibility of 83% and 99% respectively.⁵

All the patients who were treated with FT in the present study showed complete clinical and bacteriological cure. Neumann et al. also found that clinical and bacteriological cure was achieved in 17 out of 18 patients (94%) with UTI.⁶ Single dose oral treatment offered 100% compliance as observed in the present study. In overall evaluation, the most frequently observed adverse events were diarrhoea, nausea, epigastric/abdominal pain and headache. Naber et al. also demonstrated that this drug is generally safe and well tolerated.⁷

CONCLUSIONS

The results of the present study indicate the patients in the study group had better outcomes in terms of improvement of symptoms of acute lower UTI and bacteriological cure with minimum incidence of adverse drug effects. FT offers better patient compliance on the account of single oral dose. Thus fosfomycin trometamol might be considered as a promising oral antibiotic for uncomplicated urinary tract infections due to *E. coli* isolates and Enterococcus spp.

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