ORIGINAL RESEARCH PAPER

Obstetrics & Gynaecology

COMPARISON OF EFFICACY OF FOSFOMYCIN VS NITROFURANTOIN FOR URINARY TRACT INFECTION.

KEY WORDS:

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ABSTRACT

Introduction: Uncomplicated urinary tract infections (UTIs) are a common health issue, predominantly affecting women, with Escherichia coli as the primary causative agent. Fosfomycin and nitrofurantoin are recommended first-line antibiotics due to their efficacy and low resistance profiles. However, comparative studies on their clinical and microbiological outcomes are limited, necessitating further research to guide treatment decisions. **Objectives:** To evaluate the clinical and microbiological efficacy, safety, and tolerability of fosfomycin compared to nitrofurantoin in adult women with uncomplicated UTI. **Study Design:** A randomized, open-label trial was conducted at a tertiary hospital, enrolling 200 women aged 18–65 years with confirmed uncomplicated UTI. Participants were assigned 1:1 to receive either a single 3 g dose of fosfomycin or nitrofurantoin 100 mg twice daily for 5 days. Primary endpoints were clinical cure (symptom resolution) and microbiological cure (negative urine culture) at 7 days post-treatment. Secondary endpoints included adverse events and 28-day recurrence rates. **Results:** Of 200 participants, 98 received fosfomycin, and 102 received nitrofurantoin. Clinical cure rates were 91% (89/98) for fosfomycin and 88% (90/102) for nitrofurantoin (p=0.48). Microbiological cure rates were 86% (84/98) for fosfomycin and 83% (85/102) for nitrofurantoin (p=0.56). Adverse events occurred in 11% of fosfomycin patients and 14% of nitrofurantoin patients (p=0.58), primarily mild gastrointestinal issues. Recurrence rates at 28 days were 7% for fosfomycin and 9% for nitrofurantoin (p=0.68). **Discussion:** Both antibiotics showed comparable efficacy and safety, with fosfomycin's single-dose regimen offering potential advantages in patient compliance. Local resistance patterns and patient preferences should guide treatment choices. Limitations include the study's focus on non-pregnant women and open-label design. **Conclusion:** Fosfomycin and nitrofurantoin are equally effective for uncomplicated UTI, with treatment selection depending on dosing convenience, cost, and regional resistance profiles.

INTRODUCTION

Uncomplicated urinary tract infections (UTIs) are among the most frequent bacterial infections encountered in primary care, with an estimated global incidence of 150–250 million cases annually, predominantly affecting women due to anatomical predispositions such as a shorter urethra [1]. Escherichia coli accounts for 80–90% of cases, followed by other uropathogens like Klebsiella pneumoniae and Staphylococcus saprophyticus [2]. Symptoms typically include dysuria, urinary frequency, urgency, and suprapubic discomfort, without evidence of systemic illness or complicating factors such as pregnancy or structural abnormalities [3]. Effective management is critical to alleviate symptoms, prevent complications like pyelonephritis, and reduce recurrence rates, which affect up to 20–30% of women within a year [4].

Fosfomycin, a phosphonic acid derivative, and nitrofurantoin, a nitrofuran antibiotic, are widely recommended as first-line treatments for uncomplicated UTI due to their efficacy and favorable resistance profiles [5,6]. Fosfomycin is administered as a single 3 g oral dose, disrupting bacterial cell wall synthesis by inhibiting phosphoenolpyruvate transferase, and is effective against multidrug-resistant pathogens [7]. Nitrofurantoin, given as 100 mg twice daily for 5 days, damages bacterial DNA and is highly active against E. coli but less so against certain other uropathogens [8]. Both drugs are endorsed by guidelines from the Infectious Diseases Society of America (IDSA) and the European Association of Urology (EAU) for their low propensity to induce resistance compared to alternatives like fluoroquinolones [5,6].

Despite their established roles, direct comparisons of fosfomycin and nitrofurantoin are limited, with existing studies often hampered by small sample sizes or regional variations in resistance [9,10]. Factors such as dosing convenience, tolerability, and recurrence rates are critical for optimizing treatment, particularly in the context of rising antimicrobial resistance globally [11]. This study aims to compare the clinical and microbiological efficacy, safety, and tolerability of fosfomycin versus nitrofurantoin in women with uncomplicated UTI, providing evidence to inform clinical practice.

Study Design

This randomized, open-label, controlled trial was conducted at a tertiary care hospital, enrolling 200 non-pregnant women aged 18–65 years with confirmed uncomplicated UTI (clinical symptoms and positive urine culture with $\geq 10^5$ CFU/mL of a uropathogen). Patients were excluded if they had complicated UTI, pregnancy, diabetes, immunosuppression, or recent antibiotic use. Participants were randomized 1:1 to receive either a single 3 g dose of fosfomycin or nitrofurantoin 100 mg twice daily for 5 days. Randomization was performed using a computer-generated sequence. Primary outcomes were clinical cure (complete symptom resolution) and microbiological cure (negative urine culture, $<10^3$ CFU/mL) at 7 days post-treatment. Secondary outcomes included adverse events and recurrence rates at 28 days. Urine cultures were analyzed for pathogen identification and susceptibility. Data were analyzed using chi-square tests for categorical outcomes and t-tests for continuous variables, with a significance threshold of $p<0.05$.

RESULTS

A total of 200 women were enrolled, with 98 assigned to fosfomycin and 102 to nitrofurantoin. Baseline demographic characteristics were balanced between groups (Table 1). The mean age was 33.8 ± 11.9 years for fosfomycin and 35.2 ± 12.0 years for nitrofurantoin (p=0.41). Other parameters, including BMI, prior UTI history, and menopausal status, showed no significant differences (p>0.05).

Table 1: Demographic Profile Of Patients

PARAMETER	Fosfomycin(n=98)	Nitrofurantoin(n=102	P value

Age(Years, mean ± SD)	33.8 ± 11.9	35.2 ± 12.0	0.41
BMI(kg/m², mean ± SD)	24.3 ± 4.1	24.9 ± 3.9	0.32
Prior UTI history(n, %)	28 (28.6%)	33 (32.4%)	0.56
Post menopausal (n, %)	17 (17.3%)	19 (18.6%)	0.81

Table 2: Study Outcomes

PARAMETER	Fosfomycin (n=98)	Nitrofurantoin (n=102)	P value
Clinical cure rate	91% (89/98)	88% (90/102)	0.48
Microbiological cure rate	86% (84/98)	83% (85/102)	0.56
Adverse events	11% (11/98)	14% (14/102)	0.58
Reoccurrence rate	7% (7/98)	9% (9/102)	0.68

Clinical cure, defined as complete resolution of UTI symptoms at 7 days, was achieved in 89 of 98 patients (91%) in the fosfomycin group and 90 of 102 patients (88%) in the nitrofurantoin group (p=0.48)

Microbiological cure, defined as a negative urine culture at 7 days, occurred in 84 of 98 patients (86%) in the fosfomycin group and 85 of 102 patients (83%) in the nitrofurantoin group (p=0.56)

Subgroup analyses by age (<40 vs. ≥40 years), prior UTI history, and menopausal status showed no significant differences in cure rates (p>0.05 for all).

Adverse events were reported in 11% of fosfomycin patients (11/98), primarily mild diarrhoea (6 cases), nausea (4 cases), and abdominal pain (1 case), and in 14% of nitrofurantoin patients (14/102), mainly nausea (9 cases), headache (3 cases), and rash (2 cases) (p=0.58). No serious adverse events or treatment discontinuations occurred. Recurrence at 28 days was observed in 7% (7/98) of fosfomycin patients and 9% (9/102) of nitrofurantoin patients (p=0.68), with E. coli as the primary pathogen in recurrences.

Baseline urine cultures identified E. coli in 87% of fosfomycin patients and 85% of nitrofurantoin patients, followed by Klebsiella pneumoniae (8% and 9%) and other pathogens (5% and 6%). All isolates were susceptible to both drugs. Among microbiological failures (14% fosfomycin, 17% nitrofurantoin), persistent E. coli was most common, with no new resistance detected. Treatment compliance was 100% for fosfomycin and 96% for nitrofurantoin, with four patients missing 1–2 doses in the latter group. Intention-to-treat and per-protocol analyses yielded similar results.

DISCUSSION

This trial demonstrates that fosfomycin and nitrofurantoin have comparable clinical and microbiological efficacy for uncomplicated UTI in women, consistent with prior studies [9,10]. Clinical cure rates (91% vs. 88%) and microbiological cure rates (86% vs. 83%) were statistically similar, supporting their roles as first-line therapies per IDSA and EAU guidelines [5,6]. The high efficacy against E. coli, the dominant uropathogen, aligns with low resistance rates reported for both drugs [7,8].

Fosfomycin's single-dose regimen offers a practical advantage, potentially enhancing adherence, particularly in outpatient settings where compliance is a challenge [12]. Nitrofurantoin's 5-day course, while effective, requires greater patient effort, which may impact real-world outcomes [13]. Adverse events were mild and comparable (11% vs. 14%), consistent with known profiles: gastrointestinal issues for fosfomycin and nausea for nitrofurantoin [7,8]. The absence of serious adverse events supports the safety of both drugs for short-term use.

Recurrence rates (7% vs. 9%) were low and comparable, suggesting sustained efficacy, though longer follow-up is needed to assess late recurrences [4]. The predominance of E. coli in baseline and recurrent infections underscores the importance of local susceptibility data, as resistance to other agents like fluoroquinolones is rising [11]. Fosfomycin's activity against multidrug-resistant strains may be advantageous in high-resistance settings [7], though this was not a factor in our low-resistance cohort.

Limitations include the open-label design, which may introduce bias in symptom reporting, and the focus on non-pregnant women, limiting generalizability to other populations. Future studies should explore long-term outcomes, cost-effectiveness, and efficacy in resistant populations [9]. Treatment decisions should consider patient preferences, local resistance, and costs, with fosfomycin's convenience balanced against nitrofurantoin's affordability [12,13].

CONCLUSION

Fosfomycin and nitrofurantoin are equally effective and safe for uncomplicated UTI in women, with fosfomycin offering dosing convenience and nitrofurantoin providing a cost-effective option. Treatment choice should be guided by patient factors, local resistance patterns, and healthcare system considerations.

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