

COMPARATIVE ASSESSMENT OF FOSFOMYCIN AND NITROFURANTOIN THERAPY IN URINARY TRACT INFECTION DURING PREGNANCY.

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Abstract

Background: Urinary tract infections in pregnancy can be complications if the microbes causing it are proven to be resistant to standard use antibiotics. Routinely a multi-dose regimen of nitrofurantoin is used as a management protocol, however recent literatures have highlighted the relative efficacy of Fosfomycin in successful treatment. The present study was done to comparatively assess the efficacy of single dose Fosfomycin and standard dose nitrofurantoin in UTI among pregnant females, **Methodology:** Study employed a pool of 60 subjects divided equally in two groups. The groups were provided either with Fosfomycin or nitrofurantoin. **Observations:** Fosfomycin showed a lower rate of side effects and microbial resistance as compared to nitrofurantoin. The clinical and laboratory analysis revealed a statistically significant superiority of Fosfomycin in the selected study sample. **Conclusion:** Fosfomycin showed a better outcome compared to nitrofurantoin in the selected study sample.

Keywords: Fosfomycin, Nitrofurantoin, Pregnancy, UTI

Introduction

Females have a greater propensity towards urinary tract infection owing to anatomical and physiological factors that promote bacterial activity. The lower part of the urinary tract is the commonest site for such infections.¹ In females who are pregnant, this infection if not controlled in early stages can cause adverse complications which may lead to a elevation in morbidity and sometimes mortality of the unborn foetus.²

Uncomplicated lower UTI is usually defined as acute cystitis occurring with no known abnormalities of the urological tract, and is characterized by symptoms such as dysuria, urgency, frequency, suprapubic pain and/or haematuria^{1,2}

The commonest organism for causing such infections have been in the E. coli family commonly called as enterobacteriae. These organisms have recently been implicated in being responsible for a range of diseases which have shown an effective resistance against major antibiotics such as fluoroquinolones, aminoglycosides, and sulfamethoxazole- trimethoprim, and are known as multidrug-resistant organisms (MDROs)^{3,4}

Fosfomycin trometamol has been recently identified as a FDA approved drug effective in the treatment of uncomplicated urinary tract infections (UTIs). Fosfomycin has shown good in-vitro activity against

common uropathogens, including Gram positive and negative organisms such as Escherichia coli which includes extended-spectrum β -lactamase-producing E. coli, Proteus mirabilis, Klebsiella pneumoniae and Staphylococcus saprophyticus.^{5,6}

Scientific publications on the effectiveness of fosfomycin have demonstrated that the level of efficacy is comparable with long term regimes of antibiotics such as ciprofloxacin, norfloxacin, cotrimoxazole or nitrofurantoin in uncomplicated cases.^{7,8}

The present study was designed to comparatively assess the efficacy and adverse effects of Fosfomycin and nitrofurantoin in uncomplicated lower UTI cases who are pregnant.

Methodology:

The present study was a randomized prospective interventional study conducted at the department of urology in Geetanjali Medical College and Hospital, Udaipur. The study duration spanned a period of 6 months from January 2021 to June 2021. The institutional ethical clearance was obtained prior to start of the study.

The study protocol involved a pool of 60 adult subjects who were in midst of an uncomplicated pregnancy between 12- 20 weeks of gestation. All subjects were

informed of the need for the study and written informed consent in a language of their understanding was obtained from them.

The inclusion criteria were; asymptomatic bacteriuria or cystitis, Patient in whom culture revealed an antibiotic contraindicated with pregnancy.

History of congenital urogenital anomalies; hydronephrosis due to any cause, Urinary stones; Diabetic and immuno-compromised patients; Patients with high grade fever associated with flank pain and/or signs of pyelonephritis; and patients refusing consent were excluded from the study.

The subjects were divided in two equal groups randomly. Group F received oral Fosfomycin single dose therapy. Group N received oral Nitrofurantoin.

Questionnaire was designed and pre-validated by collaboration with peers. It was made of 3 sections: The first section, considered demographic data of

participants, the second sections, considered patients' presentation, symptom relief, residual symptoms, compliance and costs of treatment. The third section evaluated the efficacy of treatment by second urine analysis findings and occurrence of side effects and specifying these side effects

The data collected was subjected to statistical analysis using SPSS ver 16 software for tests of central tendency and significance.

Observations:

The data compiled revealed that there were no statistically significant differences in the demographic data of the study participants. In terms of the efficacy of management between the two test drugs, the data was collected on basis of clinical symptoms, examination, urine analysis and side effects. The data is as depicted in Table 01.

Table 2: Comparative Clinical and Laboratory Profile.

Parameter	Group F	Group N	P value
Symptomatic Improvement	30	27	<0.05
Urine Analysis (Pus Cell Count)	0-10 / HPF	12-15/ HPF	<0.05
Side Effects (No. of Patients)	4	7	<0.05
Resistance (No. of Patients)	1	5	<0.05

In terms of symptomatic improvement of the patients, Fosfomycin group patients had a better outcome, with all reporting a lack of any symptoms on day 7, while 3 subjects still had mild symptoms from the nitrofurantoin group.

In terms of side effects, the commonest symptom reported by both groups was nausea and dyspepsia, followed by diarrhoea. The incidence of adverse effects was substantially lower in the Fosfomycin group compared to the other one.

Statistical analysis revealed that there were statistically significant differences between the number of patients that had a unfavorable urine analysis report and microbial resistance to Fosfomycin and nitrofurantoin. Fosfomycin had a significantly lower incidence and a better outlook among the selected study participants.

Discussion:

Urinary tract infections (UTIs) are common among pregnant females due to associated physiological changes that favour the occurrence of UTI. Although pregnancy is a major risk factor for UTI, there are many other contributing factors such as, socioeconomic state,

diabetes mellitus, recurrent UTI, and other immunologic and blood diseases.⁹

It is reported in many studies that urine cultures can be time and money consuming, risk of contamination exists and in certain cases antibiotic sensitivity results may be inconvenient with pregnancy; these factors motivate urologists and obstetricians to initiate an empirical antibiotic therapy especially in patients who are symptomatic.¹⁰

With this in mind, a newer drug was tried. Fosfomycin trometamol is used in single dose and has shown stability with reduced appearance of mutant urinary strains overtime in many studies. It has higher efficacy and better compliance over Nitrofurantoin and other drugs making it a first choice drug for uncomplicated UTIs In pregnancy¹¹.

Usha et al, in their study reported that treatment with a single dose of Fosfomycin trometamol is as effective as the standard course of treatment with Amoxicillin-clavulanic, or cefuroxime axetil, and Fosfomycin trometamol is preferable owing to its simpler use. This is similar to our observations in the present study.¹²

Liu HY, et al and Araj GF et al. reported a vitro susceptibility to Fosfomycin of 86% - 100% more than Nitrofurantoin with comparable results between both groups. These results are comparable to result of this study where persistent infection was found in 1 case in Fosfomycin group and in 5 cases in Nitrofurantoin group.¹³

Study by Ceran N, et al. reported comparable results between Fosfomycin and ciprofloxacin with disappearance of pyuria in 80% of cases, our study had better results probably due to less use of Fosfomycin in our country with less appearance of resistant strains.¹⁴

Conclusion:

The study concludes that a better outcome, lower side effects and simpler administration modality is reason for making Fosfomycin as a better and first choice alternative when managing UTI's in pregnancy. The present study is limited by the small sample size, and further studies with better samples may be more effective in determining the efficacy.

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