

Efficacy of Fosfomycin in Urinary Tract Infections Occurring During Pregnancy

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ABSTRACT

Objective: To determine efficacy of fosfomycin in urinary tract infections occurring during pregnancy.

Study Design: Descriptive study.

Study Settings: Obstetrics & Gynecology Ward Dow University OJHA Campus, Karachi.

Duration of Study: 11-08-2021 till 12-02-2022

Subject and Methods: Total 147 pregnant women presented with urinary tract infections were enrolled. Detailed demographics were recorded after taking informed written consent. Participants were given fosfomycin sachet 3gm stat dose after confirmation of UTI symptoms and they were followed for about 13 days and advised to proceed for Urine C/S. Participants were assessed on the basis of persistent symptoms of UTI and identification of bacteria in urine C/S. Data was analyzed by SPSS 20.0.

Results: The mean age of the patients was 29.41±4.71 years. Mean BMI recorded was 28.65±3.21 kg/m². According to the efficacy of drug (fosfomycin), UTI was cured in 89 (60.5%) patients.

Conclusion: The efficacy of fosfomycin in urinary tract infections occurring during pregnancy in our study was 60.5%.

Keywords: Urinary Tract Infection (UTI), Efficacy, Fosfomycin

INTRODUCTION

Pregnancy-related urinary tract infections (UTIs) are the second most prevalent disease [1]. Infection of the urinary tract is one of the most common problems that can arise during pregnancy is a urinary tract infection (UTI). Twenty percent to forty percent of pregnant women with asymptomatic bacteriuria will develop pyelonephritis. Because women have a shorter urethra, they are more susceptible to UTIs [2]. This risk is increased by the fact that poor hygiene and urine secretions can speed up the infection process. A review found that roughly 5 percent of pregnant women were admitted to the hospital because of a urinary tract infection [3]. More people live below the poverty line in emerging countries like Pakistan [2]. Pregnancy-related UTIs are a leading cause of mother and infant morbidity and mortality. It has been observed that pyelonephritis is associated with an increased risk of preterm birth. Fetal mortality is common, as is the prevalence of babies born with low birth weight [4]. Anemia, thrombocytopenia, prenatal hypertension, transitory renal insufficiency, and postpartum endometritis are all risk factors for pyelonephritis in pregnant women [5].

Urinary tract infections (UTIs) are a common consequence of pregnancy. Bacterial cystitis is the typical clinical presentation in otherwise healthy women who have an unimpaired voiding mechanism and anatomically normal urinary tract. It appears that the infection is limited to the lower urinary tract in the vast majority of patients. It is possible for there to be no symptoms (asymptomatic bacteriuria) or for there to be acute cystitis [6]. Most typically, pregnant women will isolate *Escherichia coli* as their uropathogen of choice. Other than the Enterobacteriaceae (*Klebsiella*, *Enterobacter*, and *Proteus*), *Staphylococcus epidermidis* or *Staphylococcus saprophyticus*, *Enterococcus faecalis*, and the *B Streptococcus* group may also be to blame. Asymptomatic bacteriuria is seen in 2- 13% of pregnant women, while symptomatic infection affects 1%-2% of pregnant women, according to research conducted in the United States, Europe, and Australia [7]. Hormonal shifts and the influence of mechanical factors during pregnancy can lead to urinary tract infections (UTIs) and bacteriuria [8, 9]. These alterations can affect urinary bladder emptying, increase residual volume, and increase the prevalence of vesicoureteral reflux. After 28 days, 139 out of 241 patients had seen improvement in their symptoms and had a negative urine culture [9]. This indicates that the antibiotics were effective in 58% of the cases.

Urinary tract infections (UTIs) are prevalent and a prominent reason for prescribing antibiotics [10]. Improper use of antibiotics in the outpatient setting may contribute to the development of antibiotic resistance in the general population [11]. Emergence of multidrug-resistant uro-pathogens is a growing concern, since it poses difficulties for the use of oral antibiotics currently in use. Only a small amount of information is known for MDR or complex UTIs [12].

The development of new antibiotics effective against MDR and XDR bacteria is slow, and the spread of MDR and XDR pathogens is a major obstacle to treating bacterial illnesses. Therefore, traditional antibiotics such as polymyxins, tetracyclines, and aminoglycosides have been reintroduced by medical professionals. For its continued efficacy against multidrug-resistant and extremely resistant Gram-positive and Gram-negative bacteria, fosfomycin has recently come under scrutiny in response to the emergence of resistance to these drugs. Several questions have been answered, and new, high-quality data has been released [13].

In places where resources are scarce, it is especially important to prioritise the use of simple, cheap, and widely available methods for preventing and treating common health problems. Fosfomycin is a promising treatment for urinary tract infections in pregnant women because it meets both of these criteria. The effectiveness of fosfomycin in the treatment of urinary tract infections that arise during pregnancy has been investigated previously, but to the knowledge of the investigators, no such study has been conducted in Pakistan. Therefore, this study was conducted to produce the necessary local data in this regard to promote evidence based medicinal practise in Pakistan for the treatment of urinary tract infections, with the goal of preserving the best health for both mother and foetus.

MATERIALS AND METHODS

This descriptive study was conducted at Obstetrics & Gynecology Ward Dow University OJHA Campus, Karachi during from the period 11-08-2021 to 12-02-2022. Total 147 pregnant women with symptoms of urinary tract infections were enrolled. Patient's ages were ranging between 22 to 40 years. Pregnant mother with lower abdominal pain by any specific reason other than UTI, pregnant patient in labor, and non-pregnant women with symptoms of UTI were excluded.

The main researcher herself was in charge of gathering the data. After the patients gave written and informed consent, they were asked about their age, weight, height, trimester, co-morbidities, and symptoms of urinary tract infection before and after treatment, such as the need to go to the bathroom right away, trouble going to the bathroom, pain when going, fever, chills, etc. They took note of the patient's blood pressure, temperature, dose, duration, and how often fosfomycin was given. Any bad side effects of the medicine, like feeling sick, throwing up, having diarrhoea, having stomach pain, or getting a headache, will be written down. After confirming that the participants had UTI symptoms, they were given fosfomycin sachet 3gm stat dose. They were then watched for about 13 days and told to get a Urine C/S. The participants were evaluated based on how long their UTI symptoms lasted and how many bacteria were found in their urine C/S. The information was all kept secret. All of the information was written down by the researcher herself on pre-made forms.

SPSS version 20.0 was used to look at the data. Continuous variables like age, weight, height, trimester, and blood pressure were shown as means and standard deviations, while categorical variables like place of residence, booking status, co-morbidities, history of hypertension, diabetes, GDM, PIH, trimester of pregnancy, and previous history of abdominal/pelvic surgery, previous history of UTIs, and the organism isolated on urine culture were shown as frequencies and percentages.

The results of the study, i.e. how well fosfomycin worked, were measured by the number of patients who were completely cured of UTI after taking fosfomycin, as shown by urine cytology (CS) and the disappearance of symptoms.

RESULTS

The mean age of the patients was 29.41±4.71 years. The mean weight of the patients was 76.45±5.34 kg. The mean height of the patients was 1.63±0.06 meters. Mean parity recorded was 1.92±1.06. Mean systolic BP was 120.88±7.74mmHg. Mean diastolic BP was 79.27±4.59mmHg. Mean BMI recorded was 28.65±3.21 kg/m2 (Table 1).

Table 1: Descriptive statistics (n = 147)

| Variables | Mean | Std. Deviation |
|------------------|--------|----------------|
| Age in years | 29.41 | 4.71 |
| Weight in kg | 76.45 | 5.34 |
| Height in meters | 1.63 | 0.06 |
| Parity | 1.92 | 1.06 |
| Systolic mmHg | 120.88 | 7.74 |
| Diastolic mmHg | 79.27 | 4.59 |
| BMI | 28.65 | 3.21 |

According to trimester, 45 (30.65) patients were in their first trimester, 53 (36.1%) were in their second trimester and 49 (33.3%) were in their third trimester (Table 2). History of PIH was found in 10 (6.8%) patients (Table 3). According to history of diabetes 9 (6.1%) patients had history of diabetes (Table 4). According to previous history of hypertension 9 (6.1%) patients had previous history of diabetes (Table 5). According to previous history of UTI 10 (6.8%) patients had previous history of UTI (Table 6). According to previous history of organisms isolated in urine test E.coli was found in 69 (46.9%) patients, Staphylococcus aureus was found in 48 (32.7%) patients, Klebsiella pneumonia was found in 15 (10.25) patients and other organisms were found in 15 (10.2%) patients (Table 7). According to the efficacy of drug (fosfomycin), UTI was cured in 89 (60.5%) patients (Table 8, Figure 1).

Table 2: Trimester distribution

| Trimester | Frequency | Percent |
|-----------|-----------|---------|
| First | 45 | 30.6 |
| Second | 53 | 36.1 |
| Third | 49 | 33.3 |
| Total | 147 | 100.0 |

Table 3: Frequency of history of PIH

| PIH | Frequency | Percent |
|-------|-----------|---------|
| Yes | 10 | 6.8 |
| No | 137 | 93.2 |
| Total | 147 | 100.0 |

Table 4: Previous history of diabetes

| History of diabetes | Frequency | Percent |
|---------------------|-----------|---------|
| Yes | 9 | 6.1 |
| No | 138 | 93.9 |

Table 5: Previous history of hypertension

| History of HTN | Frequency | Percent |
|----------------|-----------|---------|
| Yes | 9 | 6.1 |
| No | 138 | 93.9 |
| Total | 147 | 100.0 |

Table 6: History of UT

| History of UTI | Frequency | Percent |
|----------------|-----------|---------|
| Yes | 10 | 6.8 |
| No | 137 | 93.2 |
| Total | 147 | 100.0 |

Table 7: History of organisms isolated in urine culture

| History of organisms isolated | Frequency | Percent |
|-------------------------------|-----------|---------|
| E. coli | 69 | 46.9 |
| Staphylococcus aureus | 48 | 32.7 |
| Klebsiella pneumoniae | 15 | 10.2 |
| Others | 15 | 10.2 |
| Total | 147 | 100.0 |

Table 8: Efficacy of drug

| Efficacy of drug | Frequency | Percent |
|------------------|-----------|---------|
| Cured | 89 | 60.5 |
| Not cured | 58 | 39.5 |
| Total | 147 | 100.0 |

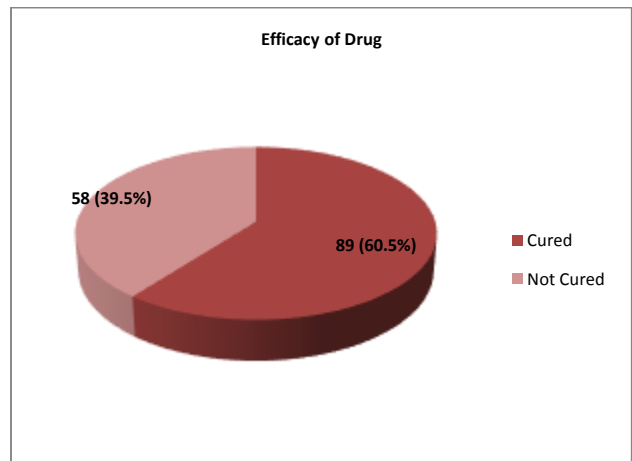


Figure 1: Efficacy of drug in enrolled patients

DISCUSSION

Fosfomycin is effective against both gram-negative and gram-positive bacteria, making it a very versatile antibiotic. High urinary fosfomycin concentrations are maintained for 2–3 days after a single dosage of fosfomycin tromethamine, and therapeutic quantities are produced in urine for 13 days. Researchers have found that treating a urinary tract infection with a single 3 g dosage of fosfomycin tromethamine is just as effective as treating it with a conventional antibiotic course of a week, including nitrofurantoin and cotrimoxazole. In addition, the FDA has approved fosfomycin for use in treating urinary tract infections in pregnant women, classifying it as a category B drug because it has similar results while causing very mild side effects [14, 15]. Thirty-two pregnant

women with lower urinary tract infections were treated by Usta et al. [16] and randomly assigned to one of three groups. Cure rates and adverse effects were comparable between the two groups. Fosfomycin trometamol, they determined, was just as efficacious as cefuroxime axetil or amoxicillin-clavulan when administered in a single dose. The adherence of fosfomycin trometamol was also improved.

Multiple medical applications for humans using fosfomycin have been studied. However, there is a paucity of information regarding the use of fosfomycin in medical interventions involving pregnant women when a single dose is required. Noreikaite et al. [17] conducted a meta-analysis and found that when comparing quinolone with fosfomycin as prophylaxis for transrectal ultrasound-guided prostate biopsy, fosfomycin had considerably less infection problems while having a similar adverse event profile. When rectal bacteria are resistant to fluoroquinolones, Besien et al [18] recommend switching to fosfomycin instead of ciprofloxacin. As a result, they reasoned, fosfomycin may be useful for treating patients who have developed resistance to fluoroquinolones. In addition, fosfomycin was shown to be as effective as parenteral cefoxitin sodium in preventing urinary tract infections following transurethral excision of bladder tumours by Yang et colleagues [19]. The use of preventive single-dose fosfomycin tromethamine for 72 endourologic surgeries was also assessed by Khawaja et al [20]. Only eight patients showed asymptomatic bacteriuria five days later. Most documented adverse effects in the medical literature were digestive system problems. According to Khawaja et al [20], the negative effects typically only lasted a short time and went away without any medicine. diarrhoea and vaginal itching were the most common adverse reactions.

The maximal concentration of fosfomycin in the plasma is detected in the urine within a few hours after dosing. Concentrations of fosfomycin in the urine were greater than 128 mg/l for at least 36 to 8 hours after a single dosing. The vast majority of bacteria and viruses that cause infections in the urinary system are effectively neutralised at these concentrations. No correlation was found between fosfomycin levels in the urine and mild renal impairment. The agony of injections, the medical necessity of injections, and the dangers associated with injections are all avoided with a single or multiple oral dose (abscesses). Our research showed that fosfomycin was 60.5% effective.

Our findings are consistent with those of a research showing that treatment with fosfomycin totally cleared UTI in 58% of patients. A single oral dose of fosfomycin was shown to kill bacteria in 96.3% of patients in a research conducted in Pakistan [20]. In another study, 89% of isolates were sensitive to fosfomycin, showing that it is a viable alternative for treating simple UTIs in pregnant women.

CONCLUSION

The efficacy of fosfomycin in urinary tract infections occurring during pregnancy in our study was 60.5%. We conclude that fosfomycin is a drug of choice for the treatment of UTI in pregnant women.

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