

ORIGINAL ARTICLE

Treatment of Acute, Uncomplicated Urinary Tract Infections in Children: A Comparison of a Single Oral Dosage of Fosfomycin Against a Seven-Day Course of Ciprofloxacin

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ABSTRACT

Objective : Urinary tract infection is one of the commonest infections in the pediatric age group. The emergence of resistance to various antibiotics has posed many difficulties in treating such patients. This study has been done to compare the efficacy of fosfomycin & ciprofloxacin in pediatric Urinary tract infection (UTI).

Study Design: Randomized Control study

Place and Duration: Akhtar Saeed Medical College/ Farooq Hospital. July, 2021 to Dec, 2021

Methodology: This randomized controlled clinical trial is done at the Department of Pediatrics, Akhtar Saeed Medical College/ Farooq Hospital. One hundred and thirty individuals who met the criteria for UTI were recruited. The patients were split into two groups at random. Patients in Group A received 15–20mg/kg of oral Ciprofloxacin twice daily (BD) for 7 days, whereas those in Group B received 150–300mg/kg of oral fosfomycin all at once.

Results: One-hundred and ten patients included in this trial. In group A mean age of the patients was 6.4±2.8 years and in group B patients had mean age 7.7±3.0 years. There were 35 males (63.6%) and 20 females (36.4%) in group A and in group B 33 males (60%) and 22 females (40%). As per effectiveness we found that fosfomycin was effective in 42 patients (76.4%) and ciprofloxacin was efficacious in 30 patients (54.5%) with p-value 0.016.

Conclusion: When comparing the treatment of children with acute uncomplicated urinary tract infections, the results showed that a single oral dosage of fosfomycin was substantially more effective than ciprofloxacin.

Keywords: Antibiotics, Resistance, uropathogens, paediatrics, UTI, gram-negative,

INTRODUCTION

UTIs are the third most common cause of fever in infants and neonates, behind ear infections and pharyngitis. It's associated with a high mortality rate and has lasting effects as well. It is a medical disorder in which bacteria live and multiply in the urinary tract (the kidneys, the ureters, and the bladder) ⁽¹⁾. Urinary tract infection describes this ailment (UTI). Following the age of 6 months, around 10% of girls and 3% of boys may get a urinary tract infection (UTI). ⁽²⁾

The short-term effects (pyelonephritis, sepsis) and long-term complications (renal failure) can be avoided with early identification and treatment (kidney scarring, hypertension, and renal failure). Most often recommended antibiotics for UTIs include: ⁽³⁾ sulfamethoxazole, trimethoprim, beta lactams, fluoroquinolones, amoxicillin, aminoglycosides, fosfomycin, and nitrofurantoin.

These days, antimicrobial resistance is a worldwide problem that everyone knows about. This issue is exacerbated by the availability of OTC medications and the careless use of antibiotics, especially in underdeveloped nations. The literature shows a rise in resistance to several antibiotics, including ampicillin (96%), cotrimoxazole (46%), amoxicillin, nalidixic acid, and co-amoxiclav. a combination of ⁽⁴⁾⁽⁵⁾⁽⁶⁾ and ciprofloxacin. ⁽⁷⁾ Because of this, current treatment methods need to be reconsidered.

Although it is one of several medications that may be used to treat urinary tract infections, fosfomycin is rarely utilised. This drug's fast absorption after oral administration, concentration for excretion in urine, and biofilm action have brought it renewed interest despite its age. ⁽⁸⁾ When taken orally, it has very few side effects (diarrhoea in about 5% of patients) and is generally well tolerated. ⁽⁹⁾⁽¹⁰⁾ It's effective against several different types of bacteria that have developed resistance to multiple different drugs, including MRSA, extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae, and AmpC-producing Enterobacteriaceae ⁽⁶⁾⁽¹¹⁾. Fosfomycin's effectiveness was found to be comparable to that of the comparative regimens in a meta-

analysis published in 2010. ⁽¹²⁾ According to research done in the United States in 2014, this medication is beneficial in treating MDR UTI. ⁽¹³⁾

There were little reports in the literature about the effectiveness of fosfomycin in treating UTI in children. Insights from this study have the potential to completely change how paediatric UT infections are treated.

METHODOLOGY

This randomised controlled trial was conducted Akhtar Saeed Medical College/ Farooq Hospital from July, 2021 to Dec, 2021. All children aged 3 to 12 with any 2 of the following symptoms— increased frequency of urination or urgency, abdominal pain (flank pain or suprapubic pain), pyuria, dysuria, with or without a fever of more than 38°C, and urine routine examination showing Pus cells> 5/HPF—were included in the study after receiving approval from the Akhtar Saeed Medical College/ Farooq Hospital Ethical Review Committee and parental consent. Participants in the trial were not permitted if they had recently taken an antibiotic, had difficulty swallowing tablets, or had an allergy to ciprofloxacin or fosfomycin. A standardised questionnaire was used to gather all of the data. The pathology lab obtained midstream urine from a clean catch for routine & culture before the initiation of antibiotic therapy. In order to rule out any potential issues with the urinary tract, a uroynecological ultrasound was conducted. One hundred thirty persons were surveyed for this study. The patients were divided into two groups at random. Patients with a non-even enrollment number were maintained in group A, whereas those with an even number were maintained in group B. Group A received oral Ciprofloxacin 20 mg/kg, BD for 7 days, whereas Group B received oral fosfomycin 300 mg/kg in a single dosage. The 5th and 10th day of therapy were used for follow-ups with the patients. In order to evaluate the efficacy of the medication, another urine R/E was performed on day 10. Clinical success was defined as a urine R/E revealing a white blood cell count (WBC) of 5 or below by day 10.

20 patients were lost to follow-up.

SPSS 22 was used for the statistical analysis. Quantitative variables were analysed by computing their means and standard deviations. Quantitative measures of frequency and proportion were derived from qualitative measures. The effectiveness of the two groups was compared using chi-square analysis. We defined statistical significance as a P-value below 0.05. Using stratification, we were able to manage the influence of age, gender, education, and socioeconomic status on the observed effects. Following stratification, a Chi-square test was performed.

RESULTS

In group A mean age of the patients was 6.4±2.8 years and in group B patients had mean age 7.7±3.0 years. Table 1 shows the gender breakdown of both sampled populations.

In 50 patients, normal urine testing revealed 20-30 pus cells, and in 20 patients, the number increased to 30-40. In 10 patients, there were 50-60 pus cells, and in 30 patients, there were more than 100 pus cells.

As per effectiveness we found that fosfomycin was more effective in 42 patients (76.4%) than ciprofloxacin in 30 patients (54.5%) with p-value 0.016 (table 2). Tables 3 and 4 illustrate the results of age and gender stratification, respectively.

Table-1: The distribution of patients by gender

Gender	Group-A (Oral Ciprofloxacin)		Group-B (Oral fosfomycin)	
	No.	%	No.	%
Male	35	63.6	33	60.0
Female	20	36.4	22	40.0
Total	55	100.0	55	100.0

Table-2: Comparison of efficacy

Efficacy	Group-A (Oral Ciprofloxacin)		Group-B (Oral fosfomycin)	
	No.	%	No.	%
Yes	30	54.5	42	76.4
No	25	45.5	13	23.6
Total	55	100.0	55	100.0

Chi-square = 5.789
P-value = 0.016

Table-3: Stratification for age

Age (Year)	Group	Efficacy		Total	P-value
		Yes	No		
≤ 5	Group-A	15	8	23	0.680
	Group-B	10	7	17	
Total		25	15	40	
≥ 6	Group-A	15	17	32	0.001
	Group-B	32	6	38	
Total		47	23	70	

Table-4: Stratification for gender

Gender	Group	Efficacy		Total	P-value
		Yes	No		
Male	Group-A	19	16	35	0.006
	Group-B	28	5	33	
Total		47	21	68	
Female	Group-A	11	9	20	0.569
	Group-B	14	8	22	
Total		25	17	42	

DISCUSSION

Children with fever often have a urinary tract infection, which is a common but often overlooked cause of illness. Since most doctors don't have a particularly high index of suspicion for UTIs in kids, many infections go untreated and can cause serious long-term damage to the child's health and quality of life. Therefore, prompt identification and treatment is essential for the avoidance of serious, long-term consequences.

In our research, the mean age of patients in groups A and B was 6.4±2.8 and 7.7±3.0 years, respectively, while a 2015 study

at the Department of microbiology in Bengaluru, Karnataka, India, found that the age range was 1–5 years. (14) Unlike our research, where boys made up the majority, this one had an even split of males (63.6% in Group A and 60% in Group B). Whereas in a research done in Istanbul, 61% of patients were female (1.5 girls: 1 boy) and the average age was 3 years and 9 months. (15) Women made up the majority of respondents in a research carried out in Kashmir. Our research found that 76.4% of participants responded well to Fosfomycin, whereas 54.5 % responded favourably to ciprofloxacin. It was determined that there was a statistically significant difference (p=0.016) between the two groups. Comparable to a 1990 research that found fosfomycin to be 80% effective, this one shows similar results. The current study's success rate of 65% for fosfomycin in MDR UTI (13) is lower than a 2016 study's success rate of 55%. In another study, researchers found that fosfomycin was effective against all samples of every species tested. (11) Because of its distinct method of action, fosfomycin seldom causes cross-resistance and can work in conjunction with other antibiotics. Not only is it effective against a wide variety of bacteria, but it is also able to kill some of the strains of bacteria that have become immune to antibiotics in recent years. Eight (6) investigations showed that fosfomycin is highly effective against E. coli (MIC 16 g/ml). (18)

Similarly, a meta-analysis also reports a significant rate of ciprofloxacin resistance in UTI, with the prevalence of this phenomenon increasing in developing countries due to the increased use of OTC antibiotics. (7) Ninety-two percent resistance to fluoroquinolones was also observed in a research from 2016. (19) In contrast to the current research's results, which demonstrate a sensitivity to ciprofloxacin of only 54.4%, Ibeneme's 2014 study revealed a sensitivity to ciprofloxacin of 81.8% (4), and Butler et al report 's of 96.2% (20). Antibiotic resistance has emerged, and antibiotic susceptibility patterns have changed, during the previous few years, as seen by this variation in sensitivity. This is supported by two studies, one from Turkey(15) and the other from Australia(21), both of which show a rising prevalence of ciprofloxacin-resistant bacteria. Naz did a local investigation and found that E. coli has developed resistance to nearly all antibiotics tested, including ciprofloxacin (46% resistance). (22)

One of the study's biggest drawbacks was how difficult it was to persuade the parents that a single dosage of oral antibiotic would cure their child's condition. Authors made every effort to ensure that all enrolled children had never been given antibiotics, however parental denial about this fact remains a potential bias source. The use of USG alone to rule out anatomical defects might also overlook certain abnormalities.

Fosfomycin is a promising new antibacterial, but there is a dearth of information comparing it to other options for use in paediatric patients. Lack of clarity on its dosing regimen, especially in babies and young children, is one of the barriers presently restricting fosfomycin's acceptance in paediatric patients; further clinical trials are needed to clarify its safety profile and optimal dose in paediatric patients. A multifaceted approach over the coming decades is needed to preserve the miracle of antimicrobials, and while re-examining 'lost' drugs like nitrofurantoin and fosfomycin is beneficial, it is just one piece of the issue.

CONCLUSION

Treatment of acute, uncomplicated urinary tract infections in children with a single oral dosage of fosfomycin was more effective than with ciprofloxacin. Fosfomycin has cheap treatment costs, a low chance of developing resistance, and high levels of patient compliance, making it an ideal medicine to employ as part of an initial empirical therapy regimen for the treatment of UTI.

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