FOSFOMYCIN VS NITROFURANTOIN AGAINST THE TREATMENT OF URINARY TRACT INFECTION IN TERTIARY CARE HOSPITAL KARACHI

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Author's Contribution:

N.A. and F.K. designed the model and the computational framework and analyzed the data. S.S.M. and H.A. carried out the implementation. F.M. performed the calculations. N.A. and F.K. wrote the manuscript with input from all authors. S.S.M and M.L. conceived the study and were in charge of overall direction and planning.

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ABSTRACT:

Aim:

To assess the compare the efficacy of Fosfomycin vs Nitrofurantoin in the treatment of urinary tract infection in tertiary care hospital.

Material and Methods:

A total of 120 urine sample were collected from patients presenting with UTI. Mueller Hinton Agar was used in the disc diffusion technique to test for antibiotic resistance. Fosfomycin (300 ug) and Nitrofurantoin (300 ug) discs were used.

Results:

The mean age of the patients were 45.94±9.49 years. The most prevalent uropathogen found were *E.coli* and *Klebsiella*. Sensitivity of isolated Uropathogens against Fosfomycin and Nitrofurantoin was 96.7% and 80%.

Conclusion:

Fosfomycin showed better efficacy as compared to Nitrofurantoin against uropathogens.

Keywords: Urinary Tract Infection, Fosfomycin, Nitrofurantoin.

INTRODUCTION:

Urinary tract infections (UTIs) are among the infections that are most often seen in clinical settings. One of the main issues is how to treat women who experience persistent UTIs [1]. However, at least one-third of infections acquired in hospitals may indeed be prevented. *Escherichia coli (E.coli)* is one of the gram-negative germs that generally results in UTIs[2]. Antimicrobial resistance has increased exponentially across several Gram-negative bacteria. Multi-drug resistance in *Enterobacteriaceae,* which causes urinary tract infections, is another issue [3]. Resistance to at least one agent in three or more antimicrobial groups is the definition of multi-drug resistance in negative isolates [4].

In the past, typical urinary tract infections have been addressed with Trimethoprim-Sulfamethoxazole and Ampicillin. Though, these treatments are consistently losing considerable efficacy [5]. Resistance has also emerged to the quinolones and extended-spectrum Cephalosporins that are prescribed as first-line treatments. Hospital-acquired organisms contain a predominance of resistance genes. The most widespread -lactamase is CTX-M-15, and this strain of uropathogenic *E. coli* has consistently been attributed to it [3, 6]. Since the conventional treatments for these infections are no longer productive. Some of the few drug treatments on the shelf have already acquired resistance. Fosfomycin and Nitrofurantoin are once again increasingly being used due to the current scenario due to their broad range of action against both gram-positive and negative bacteria [7].

Fosfomycin is a remarkable antibiotic that distinguishes chemically from every other antibacterial substance that is commonly understood. The treatment is generally considered acceptable and rarely causes negative side effects [8]. It has exhibited enhanced in vitro efficacy against *E. coli* and *Klebsiella pneumonia (K. pneumonia)* that produce ESBL, with relatively impressive activity against urinary *Enterobacteriaceae* that produce ESBL [9]. Fosfomycin is not indicated for extended therapy for severe infections because it sometimes results in the formation of bacterial resistance while the patient is undergoing treatment [10, 11]. Due to its distinct technique of action from other antimicrobials, Nitrofurantoin is bactericidal. By forming reactive intermediates as a consequence of reduction with bacterial flavoproteins, it inhibits biological reactions involving RNA and DNA synthesis, and afterward cell wall synthesis as well. Specifically, MDR urinary microorganisms are more responsive to it [12]. Interest in the usage of Fosfomycin and Nitrofurantoin has lately returned due to the worldwide concern of growing antimicrobial resistance. Therefore, the goal of this study is to compare the efficacy of Fosfomycin vs Nitrofurantoin in the treatment of urinary tract infection in tertiary care hospital in Karachi.

MATERIAL AND METHODS:

This study was conducted at a Tertiary Care Hospital of Karachi from November 2021 to May 2022. The hospital's ethical review board provided its ethical approval. A total of 120 urine samples were collected from 120 patients presenting with UTI. Demographical data and baselines characteristics were recorded of each patients. An uropathogen was described as an organism with

> 10^5 colony forming units/mL of urine and is known to be linked to UTI signs and symptoms. A urine sample was deemed contaminated and eliminated from the study if it grew more than two organisms. Mueller Hinton Agar was used in conjunction with the disc diffusion technique for the antimicrobial resistance test. The antibiotic discs of Fosfomycin (300 ug) and Nitrofurantoin (300 ug) were used.

The sample was calculated using openepi web based sample size calculator. Using the previous susceptibility rate of Nitrofurantoin 81.2%[13], 7% margin of error and 95 confidence interval the calculated sample size was 120. Non probability consecutive sampling technique was deployed.

For data analysis, we used IBM SPSS statistics 25 for Microsoft Windows based system. Numerical variables were calculated using Mean and Standard deviation while categorical variables were calculated in terms and frequency and percentages.

RESULTS:

This study was conducted on 120 patients presenting for UTI. The mean age of the patients was 45.94±9.49 years. Majority of the patients were female 89 (74.2%) as compared to male 31 (25.8%). Regarding age groups our findings reveal that majority of the patients were in the age group of 51 to 60 years 55 (45.8%). Common complaint of UTI in our study were dysuria (25%), fever (18.3%) and urgency to urinate (30.8%). (Table 1). The most prevalent Uropathogen found in our study was *E.coli* which accounted for 86 (71.7%) of all pathogen. *Klebsiella* was the second most prevalent Uropathogen (20.8%). (Table 2). Regarding the sensitivity and resistance pattern of Uropathogen against Fosfomycin can be seen at table no 3. Regarding the sensitivity and resistance pattern of uropathogen against Nitrofuratoin can be seen at table no 4. The overall sensitivity of isolated uropathogens against Fosfomycin was 96.7% and against Nitrofurantoin was 80%.

Table 1: Demographics and Baseline Characteristics

DEMOGRAPHICS		N (%)
Gender	Male	31 (25.8%)
	Female	89 (74.2%)
Age groups	20 to 30 years	10 (8.3%)
	31 to 40 years	21 (17.5%)
	41 to 50 years	24 (28.3%)
	51 to 60 years	55 (45.8%)
Dysuria		30 (25%)
Fever		22 (18.3%)
Urgency to urinate		37 (30.8%)

Table 2: Uropathogen from Urine Sample

UROPATHOGEN	N (%)
E.Coli	86 (71.7%)
Candida	3 (2.5%)
Enterococcus faecalis	4 (3.3%)
Pseudomonas	2 (1.7%)
Klebsiella	25 (20.8%)

Table 3: Sensitivity and Resistance of Uropathogen against Fosfomycin

		FOSFOMYCIN		TOTAL
		Sensitivity	Resistant	
UROPATHOGEN	*E.Coli*	84	2	86
		97.7%	2.3%	100.0%
	Candida	3	0	3
		100.0%	0.0%	100.0%
	Enterococcus faecalis	3	1	4
		75.0%	25.0%	100.0%
	Pseudomonas	2	0	2
		100.0%	0.0%	100.0%
	Klebsiella	24	1	25
		96.0%	4.0%	100.0%
TOTAL		116	4	120
		96.7%	3.3%	100.0%

Table 4: Sensitivity and Resistance of Uropathogen against Nirtrofurantoin

		NITROFURANTOIN		TOTAL
		Sensitivity	Resistant	
UROPATHOGEN	*E.Coli*	77	9	86
		89.5%	10.5%	100.0%
	Candida	2	1	3
		66.7%	33.3%	100.0%
	Enterococcus faecalis	0	4	4
		0.0%	100.0%	100.0%
	Pseudomonas	2	0	2
		100.0%	0.0%	100.0%
	Klebsiella	15	10	25
		60.0%	40.0%	100.0%
TOTAL		96	24	120
		80.0%	20.0%	100.0%

DISCUSSION:

One of the most prevalent community-acquired illnesses is urinary tract infection (UTI), which is often treated with Ciprofloxacin and Co-trimoxazole. However, there has been an upsurge in efforts to find fresh therapeutic alternatives or re-evaluate the existing drugs for the treatment of UTIs, such as Fosfomycin and Nitrofurantoin, as a result of the prevalence of drug resistance in the world. For the oral treatment of UTI, Fosfomycin and Nitrofurantoin are now being prescribed more frequently in outpatient settings. Clinical data are scarce despite the abundance of literature on the in vitro sensitivity pattern of Fosfomycin and Nitrofurantoin in UTI infections[13].

In our study, the patients presented with UTI, the prevalence of females was higher than males (74.2% vs 25.8%), which is consistent with previous research that shows females have a higher frequency of UTI than males[14]. The greater occurrence of UTI in females is due to the close proximity of the urethral meatus to the anus, shorter urethra, sexual intercourse, incontinence, and inappropriate toilet.

This study's finding of a higher incidence of UTI in the elderly (51 to 60 years, 45.8%) than in younger patients (20-30 years, 8.3%) and middle-aged patients (31 to 40 years, 17.5%) are in agreement with a study by Bitew A et al[15], they reported higher frequency of UTI in elderly patients. Our findings are also consistent with a study conducted in Japan over a 20-year period that found a trend of rising complex UTI in senior individuals[16].

The most prevalent isolated bacteria were found to be *E. coli* (71.7%) and *Klebsiella* (20.8%). Other isolated bacteria from UTI cases in this study were *Candida* (2.5%), *Enterococcus faecalis* (3.3%) and *Pseudomonas* (1.7%). Various studies have reported that *E.coli* is the most prevalent isolated bacteria found in UTI followed by *Klebsiella*.[17, 18].

In our study, out of 120 gram negative urinary isolates, *E. coli* and *Klebsiella* were predominant (71.7% and 20.8%). A study from Iran found 46.6% *K. pneumoniae* and 50% *E. coli*[19]. A second study from the USA found that *K. pneumoniae* was present in 5% of cases and E. coli was prevalent in 76% of cases.[20] According to a study, *E. col*i was prevalent in Ethiopia at 94.6% and *K. pneumoniae* at 80%, whereas *E. coli* was prevalent in Nepal at 74% and *K. pneumoniae* at 44%.[21,22] The greater rates in these earlier research could be attributed to regional genetic, geographic, and socioeconomic variables.

Better susceptibility results of Fosfomycin in present study as compared to Nitrofurantoin against gram negative urinary isolates have backed up the use of Fosfomycin. About 97.7% of *E. coli* isolates were susceptible to Fosfomycin and 89.5% to Nitrofurantoin in our study. Our results are in agreement with a study[17] conducted in Pakistan which reported 95.8% sensitivity of Fosfomycin to *E.coli* isolates and 91.9% sensitivity of Nitrofurantoin.

In our study, the overall sensitivity of isolated uropathogens against Fosfomycin was 96.7% and against Nitrofurantoin was 80%. A study[13] conducted in India demonstrated similar results, they overall sensitivity of common uropathogen against Fosfomycin in their study was 99.3% and against Nitrofurantoin was 81.2%. Our findings regarding the sensitivity of uropathogens against Fosfomycin and Nitrofurantoin are also supported by various studies.[23,24]

Studies on Fosfomycin from various parts of the world have revealed that the level of drug resistance is still quite low. *E.Coli*, *Candida*, *Enterococcus faecalis*, *Pseudomonas* and *Klebsiella*, all are susceptible to its broad spectrum activity. In comparison to Nitrofurantoin, it has reduced adverse effects and effective tissue penetration with a single oral dose[25]. More clinical trials are required to confirm these medicines' efficacy in vivo because these in vitro results are preliminary.

CONCLUSION:

From our study we conclude that the isolated uropathogens showed 96.7% sensitivity against Fosfomycin and 80% against Nitrofurantoin. Therefore keeping in observation its better sensitivity we recommend Fosfomycin as a drug of choice for Urinary Tract Infection.

CONFLICTS OF INTEREST:

The authors reflect no conflict of interest.

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