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Original Article

Susceptibility Pattern of Fosfomycin from Urinary Isolates in a Private Diagnostic Centre of Central Madhya Pradesh

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Abstract

Introduction: Urinary tract infection (UTI) in a very common bacterial infection in both sexes and all age groups and is also a major cause of hospitalization. E.coli is the most common causative organism in UTI with almost 85% isolates being E.coli . The main aim of antibiotic treatment is to completely eliminate the bacteria from the urinary tract. However, with the changing pattern of antibiotic sensitivity of urinary pathogens to commonly used antibiotics and the emergence of ESBL producing E.coli the situation has worsened. A new drug, Fosfomycin , has now been frequently used as an alternative drug in the treatment of uncomplicated UTI. The present study was carried out in our microbiology department with the aim of finding out the susceptibility pattern of Fosfomycin to frequently isolated urinary pathogens. *Materials and Methods:* This was a retrospective study and urine culture of patients from January to December 2015 were included in the study. A total of 2759 urine cultures of all ages and both sexes were included in the study. All urine specimens were inoculated on Blood and MacConkey agar plates and incubated at 37^0C for 24 hours .A growth of $>10^5$CFU/ml of bacteria was labelled as significant and was further processed.The bacteria were identified on the basis of Gram staining and colony morphology and accordingly the panel for identification & susceptibility was chosen to be processed on Vitek II ((Biomerieux). *Results:* Out of 2759 urine cultures ,1341 (48.6%) cultures showed growth of bacteria. 1418 (51.3%) cultures were sterile .E. Coli (86.7%) was the commonest organism in followed by Klebsiella (8.50%), Pseudomonas (2.53%), Staphylococcus (1.41%),Enterococci (0.67%) and Proteus (0.14%). Highest sensitivity(100%) was observed in Proteus,followed by Pseudomonas(82.3%), Klebsiella(73.6%), Enterococci(66.6%) E.Coli(57.6%),and least for Staph.aureus(51.8%). *Conclusion:* The presence study suggests that resistance to Fosfomycin is on the rise and should be used with caution and resistance pattern should be monitored periodically.

Keywords: Fosfomycin; UTI; Antibiotic Susceptibility.

Introduction

Urinary tract infection (UTI) in a very common bacterial infection in both sexes and all age groups with females accounting for greater incidence of UTI because of their short urethra. It is a also a major cause of hospitalization. It has been estimated that 1 in 5 women develop UTI during their lifetime and 34% adult over the age of 20 years develop UTI once in their life time [1,2,3]. Although UTI is a benign illness with no long term medical consequences but

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it increases the risk of developing pyelonephritis ,premature delivery, increases fetal mortality among pregnant women and also impairment of renal function and end stage renal disease. E.coli is the most common causative organism in UTI with almost 85% isolates being E.coli. Other pathogens include enterobacteriaceae like Klebsiella, Proteus etc. Enterobacteriaceae are the most common organisms isolated from uncomplicated UTI in children [4-8]. The main aim of antibiotic treatment is to completely eliminate the bacteria from the urinary tract. However, with the changing pattern of antibiotic sensitivity of urinary pathogens to commonly used antibiotics and the emergence of ESBL producing E.coli the situation has worsened [9-12].

A new drug, Fosfomycin ,has now been frequently used as an alternative drug in the treatment of uncomplicated UTI. Fosfomycin is a broad spectrum phosphoenol pyruvate analog which acts by preventing the cell wall synthesis of bacteria by inhibiting UDP-N- acetyl glucosamine enolpyruvyl transferase (MurA) enzyme. The major advantage of Fosfomycin is that it is given as a single dose and has rare side effects and low resistance rates till date [12,13] .

The present study was carried out in our microbiology department with the aim of finding out the susceptibility pattern of Fosfomycin to frequently isolated urinary pathogens, specially enterbacteriaceae.

Materials and Methods

This was a retrospective study and urine culture of patients from January to December 2015 were included in the study. A total of 2759 urine cultures of all ages and both sexes were included in the study.

All 2759 urine specimens were collected by standard clean catch mid stream protocol and for catheterized patients samples were collected in sterile screw capped wide mouth container after clamping the catheter for 30 minutes. All urine specimens were inoculated on Blood and MacConkey agar plates and incubated at 37^0C for 24 hours. A routine urine examination was done to test for presence of white blood cells and bacteria in fully automated urine analyser (Beckman Coulter). Plates were observed for bacterial growth and a growth of $>10^5$CFU/ml of bacteria was labelled as significant and was further processed.

The bacteria were identified on the basis of Gram staining and colony morphology and accordingly the panel for identification & susceptibility was chosen to be processed on Vitek II (Biomerieux).

Results

The 2759 patients were divided into 0-20,21-40,41-60,61-80 And > 80 age groups.There were 40.30 % males and 59.7% females.Maximum females were in reproductive age group (700/2749) i.e. 21-40 years of age followed by 41-60 years (370/2759) and lowest in >80 years of age. The M:F ratio was 2:3. The demographic data of patients is shown in Table 1.

Out of 2759 urine cultures, 1341 (48.6%) cultures showed growth of bacteria. 1418 (51.3%) cultures were sterile. E. Coli (86.7%) was the commonest organism in followed by Klebsiella (8.50%), Pseudomonas (2.53%), Staphylococcus (1.41%), Enterococci (0.67%) and Proteus (0.14%).

Out of 1163 E.coli isolates, 57.6% isolates showed sensitivity to Fosfomycin while 42.1% were resistant.

Out of 114 Klebsiella isolates, 73.6%were sensitive to Fosfomycin and 26.3% were resistant.

82.3% Pseudomonas isolates were sensitive to Fosfomycin while 17.6 % were resistant.

66.6% Enterococci showed sensitivity to Fosfomycin and 33.3% were resistant.

51.8%Staphylococcus isolates were sensitive while 48.2% were resistant to Fosfomycin.

Proteus showed 100% sensitivity to Fosfomycin.No resistant case was observed in this isolate.The MIC value and sensitivity percentage is shown in Table 3 .

Highest sensitivity(100%) was observed in Proteus, followed by PSeudomonas (82.3%), Klebsiella (73.6%), Enterococci (66.6%) E.Coli (57.6%), and least for Staph. aureus (51.8%)

Table 1: Showing demographic data of patients N= 2759

Age in years	Male	Female
0 - 20	300	350
21 - 40	200	700
41 - 60	310	370
61 - 80	248	200
> 80	55	26
Total	1113	1646
Percentage	40.30%	59.70%

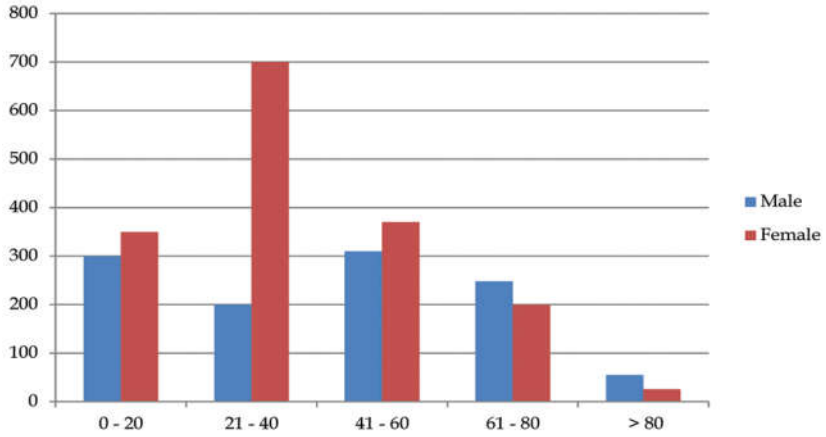

Fig. 1: Showing demographics of patients

Table 2: Showing percentage of different isolates N= 2759 Cultures

Organisms	Total Isolated	Percentage
E.coli	1163	86.70%
Klebsiella	114	8.50%
Pseudomonas	34	2.53%
Proteus	2	0.14%
Staphauerus	19	1.41%
Enterococci	9	0.67%
Sterile	1418	51.30%
Total positive	1341	48.60%

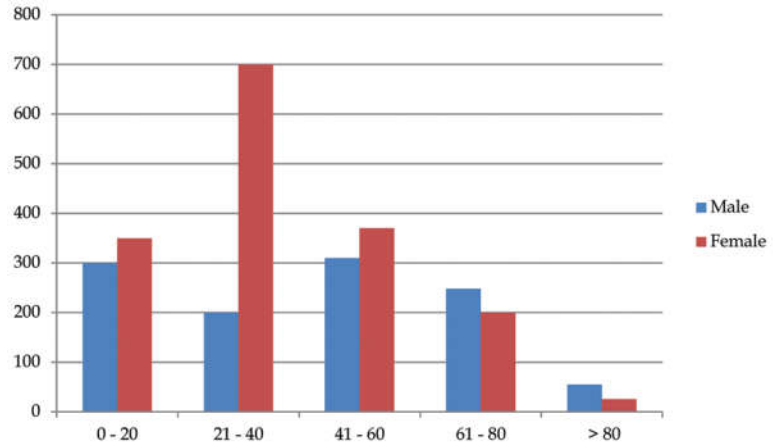

Fig. 2: Showing percentage of different isolates

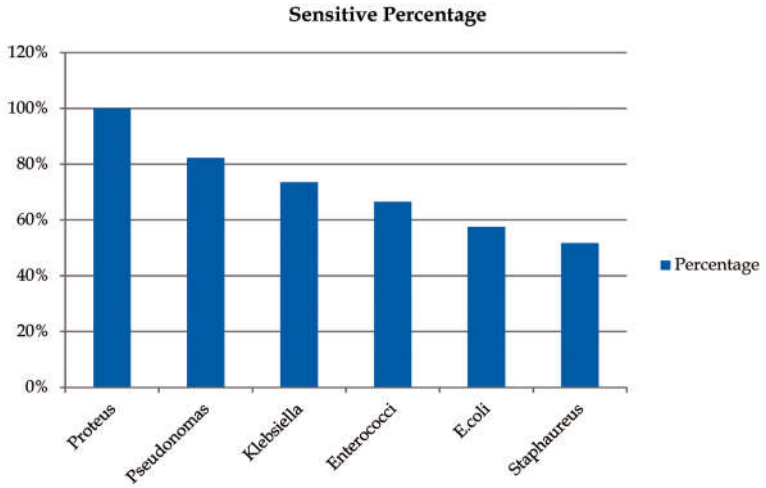

Fig. 3: showing percentage of fosfomycin sensitive isolates

Table 3: Showing sensitive and resistance percentage of isolates

Organisms	FOS- Sensitive	Percentage	Sensitive MIC	FOS- Resistant	Percentage	Resistant MIC	Total
E.coli	670	57.60%	<=16	493	42.30%	>=256	1163
Klebsiella	84	73.60%	<=16	30	26.30%	>=256	114
Pseudonomas	28	82.30%	<=16	6	17.60%	>=256	34
Enterococci	6	66.60%	<=16	3	48.20%	>=256	19
Staphaureus	11	51.80%	<=16	8	33.30%	>=256	9
Proteus	2	100%	<=16	0	0	>=256	2
Total	801	59.70%		540	40.20%		1341

Resistant Percentage

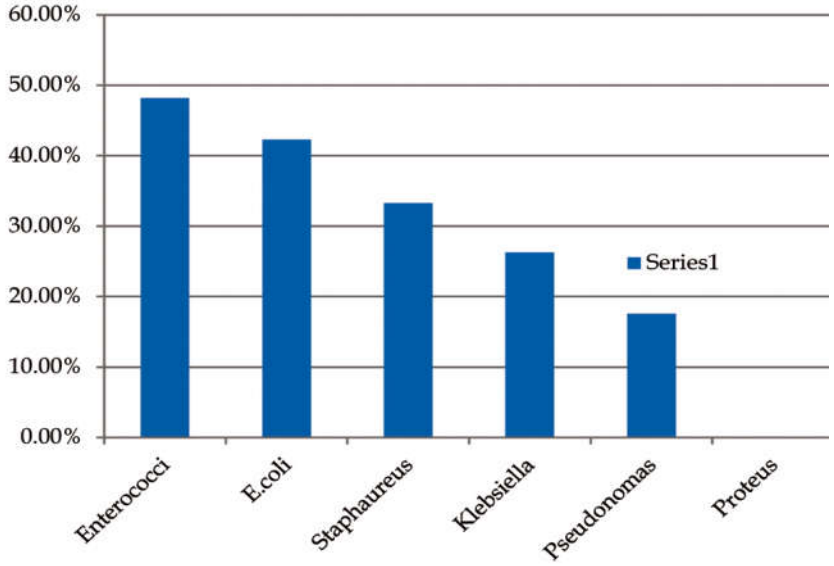

Fig. 4: showing percentage of fosfomycin resistant isolates

Discussion

Enterobacteriaceae are the most common isolates found in uncomplicated UTIs. UTIs have become increasingly difficult to treat and eradicate due to growing antibiotic resistance to commonly used antibiotics. TekinTas et al found a resistance rate of 1.9% to Fosfomycin in their study [15]. Other studies have revealed resistance to Fosfomycin between 1.2-4.5% [16-19].

Resistance to Fosfomycin rarely develops and is mostly chromosomal or plasmid mediated.The chromosomal resistance is caused by mutations in structural genes which code bacterial proteins helping to transport the agent in to the cell [20].

Fosfomycin is approved in many countries worldwide for the treatment of uncomplicated UTIs. It has a good in vitro activity against E. Coli,ESBL producing E. Coli,Proteus, Klebsiella and Staphylococcus. A single dose of Fosfomycin achieves good concentration in urine and has similar efficacy to 3-7 days regimen of other common urinary antibiotics like Norfloxacin,Nitrofurantoin Ciprofloxacin. The only known side effect of Fosfomycin is gastro intestinal disturbances like diarrhea and nausea. In our study, the resistance rate to Fosfomycin was quite high. 40.2% total isolates showed resistance to Fosfomycin with Staphylococci accounting for highest resistance (48.2%),followed by E.Coli(42.3%), Enterococci(33.3%), Klebsiella(26.3%) Pseudomonas(17.6%). This is an alarming sign.

Conclusion

The presence study suggests that resistance to Fosfomycin , an antibiotic of choice in UTIS because of its single dose regimen and very few side effects, is on the rise and should be used with caution and resistance pattern should be monitored periodically.

Conflict of Interest

none

References

1. Schappert SM. Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 1995. Vital Health Stat. 1997; 13(129): l-38.
2. Griebling TL (2013) Urologic Diseases in America. Urinary Tract Infection in Women Chapter 18: 589-617.
3. U.S. Department of Health and Human Services. Kidney and Urologic Diseases Statistics for the United States: National Kidney and Urologic Diseases Information Clearinghouse, National Institutes of Health NIH Publication No. 10–3895; 2010.
4. DeAlleaume L, Tweed EM, Bonacci R. When are empiric antibiotics appropriate for urinary tract infection symptoms? J Fam Pract. 2006; 55: 341-342.
5. Wilson ML, Gaido L. Laboratory Diagnosis of Urinary Tract Infections in Adult Patients. Clin Infect Dis. 2004; 38: 1150-1158.
6. Akram Md, Shahid Md, Khan AU (2007) Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in J N M C Hospital Aligarh, India. Annals of Clinical Microbiology and Antimicrobials 6:4.
7. Karlowsky JA, Lagacé-Wiens PRS, Simner PJ, DeCorby MR, Adam HR. Antimicrobial Resistance in Urinary Tract Pathogens in Canada from 2007 to 2009: CANWARD Surveillance Study. Antimicrob Agents Chemother. 2011; 55: 3169-3175.
8. Ladhani S, Gransden W. Increasing antibiotic resistance among urinary tract isolates. Arch Dis Child. 2003; 88: 444-445.
9. Ram S, Gupta R, Gaheer M.Emerging antibiotic resistance pattern in uropathogens Indian J Med Sci. 2000 Sep; 54(9): 388-94.
10. Le TP, Miller LG. Empirical Therapy for Uncomplicated Urinary Tract Infections in an Era of Increasing Antimicrobial Resistance: A Decision and Cost Analysis. Therapy for UTIs and Increases in Infectious Diseases Society of America Resistance. 2001; 33: 615-621.
11. Eryýlmaz M, Bozkurt ME, Yildiz MM, Akin A. Antimicrobial Resistance of Urinary Escherichia coli Isolates. Tropical Journal of Pharmaceutical Research Pharmacotherapy Group. 2010; 9: 205-209.
12. Aypak C, Altunsoy A, Düzgün N. Empiric antibiotic therapy in acute uncomplicated urinary tract infections and fluoroquinolone resistance: a prospective observational study. Ann Clin Microbiol Antimicrob. 2009; 8: 27.
13. Eschenburg S, Priestman M, Schonbrunn E. Evidence that the fosfomycin target Cys115 in UDPN-acetylglucosamine enolpyruvyl transferase (MurA) is essential for product release. J Biol Chem. 2005; 280: 3757-63.
14. Schito GC. Why fosfomycin trometamol as first line therapy for uncomplicated UTI? Int J Antimicrob Agent. 2003; 22: 79-83.
15. Tekin Tas, Zafer Mengeloglu, Esra Kocoglu, Özlem Bucak: In vitro activity of fosfomycin against Escherichia coli strains isolated from recurrent urinary tract infections South Eastern Europe Health Sciences Journal (SEEHSJ), Volume 3, Number 2, November 2013.
16. De Backer D, Christiaens T, Heytens S, De Sutter A, Stobberingh EE, Verschraegen G. Evolution of bacterial susceptibility pattern of Escherichia coliin uncomplicated urinary tract infections in a country with high antibiotic consumption: a comparison of two surveys with a 10 year interval. J Antimicrob Chemother. 2008; 62: 364-8.
17. Kahlmeter G. Prevalence and antimicrobial susceptibility of pathogens in uncomplicated cystitis in Europe. The ECO.SENS study. Int J Antimicrob Agents. 2003; 22: 49-52.
18. Liu HY, Lin HC, Lin YC, Yu SH, Wu WH, Lee YJ. Antimicrobial susceptibilities of urinary extendedspectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae to fosfomycin and nitrofurantoin in a teaching hospital in Taiwan. J Microbiol Immunol Infect. 2011; 44: 364-8.
19. Schmiemann G, Gágyor I, Hummers-Pradier E, Bleidorn J. Resistance profiles of urinary tract infections in general practice - an observational study. BMC Urol. 2012; 12: 33.
20. Baylan O. Fosfomycin: past, present and future. Mikrobiyol Bul. 2010; 44: 311-21. 5.