Original Research Article

**Determination of nitrofurantoin and fosfomycin susceptibility among urinary *Escherichia coli* isolates**

Rachana Kanaujia¹, Amit Kumar²*, Malay Bajpai³

¹Department of Microbiology, Homi Bhabha Cancer Hospital, Varanasi, Uttar Pradesh, India
²Department of Microbiology, Rama Medical College Hospital and Research Centre, Hapur, Uttar Pradesh, India
³Department of Pathology, Santosh Medical College and Hospital, Ghaziabad, Uttar Pradesh, India

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*Correspondence:
Dr. Amit Kumar,
E-mail: dramitgupta87@gmail.com

ABSTRACT

**Background:** Urinary tract infections (UTIs) are one of the most common infections. For treatment of UTIs, there are limited antibiotics due to increased resistance among uropathogens. Two older antibiotics; Nitrofurantoin and Fosfomycin have become novel oral therapeutic options against uropathogens. Aim of the study was to identify UTI causing micro-organisms and evaluate in-vitro activity of nitrofurantoin and fosfomycin against most common isolated organism (*E. coli*).

**Methods:** Results of urine samples culture and susceptibility testing over a period of 1 year were analysed and included in this study.

**Results:** Micro-organisms were isolated from 568 urine samples. Most commonly isolated organism was *Escherichia coli* (40.50%), followed by *Klebsiella* spp. (20.07%) and *Staphylococcus* spp. (17.07%). Susceptibility of *E. coli* to nitrofurantoin and fosfomycin was 91.74% and 65.65% respectively.

**Conclusion:** Good activity of nitrofurantoin and fosfomycin against *E. coli* indicates that these two drugs are potential therapeutic alternatives for urinary tract infections.

**Keywords:** Urinary tract infections, *E. coli*, Nitrofurantoin, Fosfomycin

INTRODUCTION

Urinary tract infections (UTI) are one of the most common infections, affecting people from all population and age groups. It accounts for 25% of all infections.¹ Every year approximately 150 million people are diagnosed with urinary tract infection worldwide.²

Usually UTI is managed empirically, leading to antimicrobial agents misuse, development of multi-drug resistance among urinary pathogens and failure of empirical therapy. Empirical antimicrobial agent selection may be determined on the basis of most likely urinary pathogen and its expected susceptibility pattern. Distribution of urinary pathogen and susceptibility to antibiotics varies in different geographic area and time to time. So periodic monitoring of UTI causing organisms and their susceptibility pattern is necessary for effective empirical treatment and management of patients with urinary tract infection.³⁻⁵

Due to lack of effective therapeutic alternatives to treat multi-drug-resistant infections, old antibiotics like nitrofurantoin, fosfomycin, have become important. Nitrofurantoin, fosfomycin are oral antibiotics and attain high concentrations in the urinary tract with minimal systemic effect.⁶⁻⁷

Objective of this study was to determine UTI causing pathogens in patients at a tertiary care center and in vitro
susceptibility of most commonly isolated micro-organism to fosfomycin and nitrofurantoin to choose for empirical treatment of UTI.

METHOD

Study design

The Present study is a retrospective study on UTI in which analysis of urinary culture results is done. This study was conducted at the Microbiology department of Rama Medical College, Hospital & Research Centre, Hapur, U.P. Data of micro-organism isolated from urine culture and the antimicrobial susceptibility profiles were collected from the records. Then data were entered into Excel and statistical analysis was done.

Microbiological methods

All the urine specimens were submitted in sterile wide mouth, screw capped container and processed within 30 minutes of collection.

Urinary routine microscopy

Urine specimens were screened manually under high power objective (400X) of optical microscope for presence of leucocytes, RBCs, casts, crystals, bacteria, and budding yeast like cells.

Culture and isolate identification

Urine samples were inoculated on cysteine lactose electrolyte-deficient medium (CLED agar, Hi-Media, India) using semi-quantitative techniques and incubated aerobically at 37 °C for 18-24 hrs. Cultures were examined for growth and colonies counted for determination of significant bacteriuria.

A growth of ≥10^5 CFU/ml was considered as significant bacteriuria, suggestive of UTI. Isolates were identified by standard biochemical procedures. Only a single positive culture per patient was included in the analysis.

Antimicrobial susceptibility tests

Antimicrobial Susceptibility Tests were done on Mueller Hinton agar medium as per Kirby-Bauer disk diffusion method. Nitrofurantoin (300 μg), Fosfomycin (200 μg) were tested against urinary Escherichia coli isolates. Results were analyzed according to Clinical and Laboratory Standards Institute (CLSI) 2018 guidelines. E. coli ATCC 25922 was used as quality control strain.

RESULT

A total of 568 bacterial strains were isolated from the urine samples of indoor patients, who were admitted to the hospital from 1st December 2017 to 30th November 2018. of these 568 patients with significant growth of organisms, 374 (65.85%) were male and 194 (34.15%) were female. Total 39 (6.87%) were of pediatric age group (<18 years) and rest 529 (93.13%) were of adult population. Gram negative bacilli (n=407) (71.65%) isolates were more than Gram positive cocci (n=161) (28.35%). Escherichia coli (n=230) (40.50%) was the most common isolated organism, followed by Klebsiella pneumoniae (n=114) (20.07%) and Staphylococcus aureus (n=97) (17.07%) (Table1).

Table 1: Bacterial isolates from urine.

| Bacterial Isolates     | No. of Strains | Percentage |
|------------------------|----------------|------------|
| Escherichia coli       | 230            | 40.50%     |
| Klebsiella pneumoniae  | 114            | 20.07%     |
| Staphylococcus aureus  | 97             | 17.07%     |
| Enterococcus species   | 39             | 6.87%      |
| Citrobacter species    | 33             | 5.81%      |
| Coagulase negative     |                |            |
| Staphylococcus species | 25             | 4.40%      |
| Pseudomonas species    | 23             | 4.05%      |
| Proteus species        | 07             | 1.23%      |
| Total                  | 568            | 100%       |

Among all isolated Escherichia coli (230), Nitrofurantoin susceptible strains were 211 (91.74%) and Fosfomycin susceptible were 151 (65.65%) (Table 2).

Table 2: Nitrofurantoin and Fosfomycin Susceptibility among Escherichia coli isolates.

| Susceptibility | Nitrofurantoin | Fosfomycin |
|----------------|----------------|------------|
| Susceptible    | 211 (91.74%)   | 151 (65.65%)|
| Resistant      | 19 (8.26%)     | 79 (34.35%) |

Three (1.30%) isolates were resistant to nitrofurantoin only and 66 (28.70%) were resistant to fosfomycin only. Total 16 (6.95%) isolates were resistant to both the drugs.

DISCUSSION

Urinary tract infection is one of the most common infectious diseases worldwide. In the present study, Gram negative bacilli (71.65%), contributed more of the total bacterial isolates than gram positive cocci (28.35%) in causing UTI. Escherichia coli (40.50%) was the most common isolated bacteria and Klebsiella pneumoniae was the second most frequently isolated organism. These results were consistent with previous studies by Kothari et al, Pardeshi et al, Akram et al, Karishetti et al, Banerjee et al, Vijayaganapathy et al, where 68%, 53.77%, 61%, 56.60%, 60.67%, 66.6% isolates were E. coli and 16.9%, 27.4%, 22%, 13%, 18.82%, 15.7% isolates were K. pneumoniae respectively. Most common UTI causing gram positive organism was found to be Staphylococcus aureus (17.07%) in this study, similar to results of studies by Pardeshi et al, Devanand et al while...
in other studies it was Enterococcus spp., followed by Staphylococcus aureus.3,9,10,12

In the present study, E. coli isolates were having good in-vitro susceptibility for nitrofurantoin (91.74%), which is quite high compared to some previous studies which was found to be 75.6% (Kothari et al), 79.62% (Pardeshi et al), 72.33%, (Patel et al), 82.3% (Sardar et al), 20% (Akram et al), 74.24 (Devanand et al),2,3,5,6,8,12

In this study Fosfomycin susceptibility against E.coli was 65.65%, which was found to be more susceptible in various other studies, 100% (Sardar et al, and Maraki et al) 98.14% Banerjee et al, 99.6% Udyan et al.6,10,13,14 Reason may be excessive use of drug in some regions which may have led to resistance to fosfomycin.

CONCLUSION

In the present study, Nitrofurantoin shows good in vitro activity against most common isolate of urinary pathogen than fosfomycin. But fosfomycin is more convenient to take as it is available in oral, single dose formulation. Both the drugs have potential to be used for empirical treatment of UTI. However, further studies are required to evaluate the in vitro resistance profiles of fosfomycin and nitrofurantoin among uropathogens.

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