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Susceptibility of Fosfomycin and Nitrofurantoin in Gram Negative Uropathogens

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Abstract **Original Research Article**

Urinary tract infections are the most common infections encountered in hospitals. With the increase in antibiotic resistant isolates, old antibiotics like Fosfomycin and Nitrofurantoin have gained importance. The present study was undertaken to evaluate the susceptibility patterns of Fosfomycin and Nitrofurantoin among the Gram negative uropathogens and also among the Extended Spectrum Beta Lactamase producers. A total of 201 mid-stream urine samples were processed by conventional methods. Identification of pathogens was done by standard biochemical tests and antimicrobial susceptibility testing was done by Kirby-Bauer's disc diffusion method and ESBL production was confirmed by combination disc test as per CLSI guidelines. Out of 201 urine samples, 73 samples were culture positive for Gram negative bacilli. Most common isolate was Escherichia coli (46.6%), followed by Klebsiella species (24.7%), Citrobacter spp (12.3%), Pseudomonas aeruginosa (8.2%), Proteus species (4.1%), Acinetobacter spp(4.1%). ESBL producers were 46.6%. In the present study, overall sensitivity to Fosfomycin was 100% whereas Nitrofurantoin was sensitive in 83.5% isolates. In our study, most of the uropathogens including the ESBL producers showed high susceptibilities to Fosfomycin and Nitrofurantoin. Therefore their role in empirical treatment of uncomplicated UTI's should be considered.

Keywords: Fosfomycin, Nitrofurantoin, susceptibility, uropathogens.

INTRODUCTION

Urinary tract infections are the most common infections encountered in hospitals. High prevalence of infection, irrational use, over-the counter availability of antibiotics, and poor infection prevention practices lead to emergence of multi drug resistance [1].

Extended-spectrum beta-lactamase production reduces the number of therapeutic options for the infection caused by these pathogens [2, 3]. The ESBL producers can also develop co-resistance to other classes of antimicrobial agents, such as co-trimoxazole, fluoroquinolones and aminoglycosides,[4] which are frequently used for UTI. Drug resistance among Gram-negative pathogens is a risk factor for inappropriate empiric treatment (IET), which in turn increases the risk for mortality.

Nitrofurantoin is a bactericidal agent. Fosfomycin is bactericidal, inhibits cell wall synthesis and has a wide spectrum of antimicrobial activity, both to Gram-negative and Gram-positive bacteria [5]. It is orally available, well tolerated and has a low incidence of harmful side-effects [6]. It was used for many years as a highly effective antimicrobial drug especially for the treatment of UTIs, but with the advent of new antibiotics such as β-lactams or fluoroquinolones, it became somewhat obsolete.

In the past decade there have been reports of a rapid increase in resistant pathogens. Hence, old antibiotics like Fosfomycin and Nitrofurantoin have gained importance.

The present study was undertaken to evaluate the susceptibility patterns of Fosfomycin and Nitrofurantoin among the Gram negative uropathogens, and to evaluate the susceptibility patterns of Fosfomycin and Nitrofurantoin among the ESBL producers.

MATERIALS AND METHODS

The present study was undertaken in the Department of Microbiology, Rangaraya Medical College, and Kakinada from July 2018 to Oct 2018. A total of 201 mid-stream urine samples were collected from patients with urinary tract infection and were inoculated onto CLED medium. The isolates obtained

were identified by standard biochemical tests and antimicrobial susceptibility testing was done by Kirby-Bauer disc diffusion method as per CLSI guidelines. ESBL production was confirmed by combination disc test using ceftazidime and ceftazidime + clavulanic acid. A difference of 5mm or more than 5mm increase in zone diameter with clavulanic acid is taken as positive for ESBL production.

Inclusion criteria

Urine cultures showing significant pure growth.

Exclusion criteria

Urine cultures showing mixed growth, and insignificant growth.

RESULTS

Among the 201 urine samples, 73 showed significant pure growth for Gram negative bacilli and were included in the study. Table 1 shows the distribution of isolates of which Escherichia coli is predominant. Figure 1 show the overall susceptibility percentage of all the isolates to various antibiotics in which susceptibility to Fosfomycin was 100% and that to Nitrofurantoin was 83.5%. Among the 73 isolates, 34(46.6%) were positive for ESBL production, of which 18 were Escherichia coli and 10 were Klebsiella species. ESBL E.coli was 100% susceptible to Fosfomycin and 77.8% susceptible to Nitrofurantoin. ESBL Klebsiella sp was 100% susceptible to Fosfomycin and 70% susceptible to Nitrofurantoin.

Table-1: Distribution of isolates

S.No.	Isolate	Number	Percentage
1	Escherichia coli	34	46.6%
2	Klebsiella species	18	24.7%
3	Citrobacter species	09	12.3%
4	Pseudomonas aeruginosa	06	8.2%
5	Proteus species	03	4.1%
6	Acinetobacter species	03	4.1%

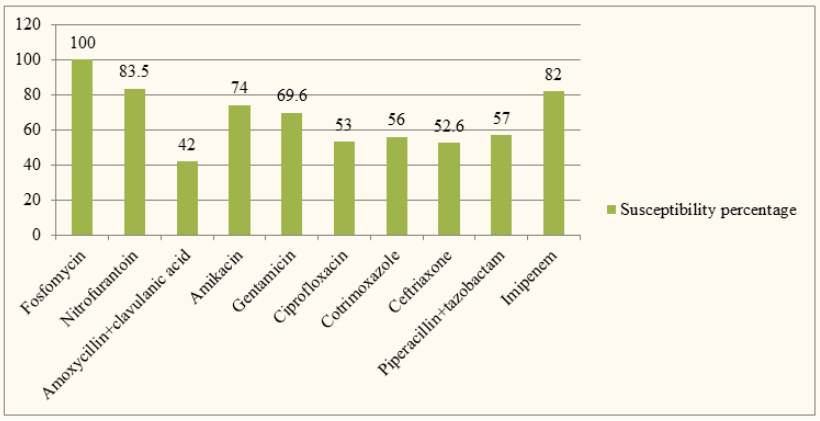

Fig-1: Antibiotic susceptibility pattern of the isolates (n=73)

DISCUSSION

Urinary tract infections are the second most common after respiratory tract infection in community acquired infections [7]. In the present study, Escherichia coli were the most common isolate followed by Klebsiella species. Studies done by Bano *et al*. Bahadin *et al*. also showed that E.coli and Klebsiella spp. are still the commonest uropathogens isolated in UTI patients [8,9].

In the present study, susceptibility of all isolates to Fosfomycin was 100% and to Nitrofurantoin were 83.5% which correlates with Madhuri *et al*. who showed 100% susceptibility to Fosfomycin and 84.76% to Nitrofurantoin against E.coli and Klebsiella [10].

Nadia *et al*. reported 98% susceptibility for Fosfomycin and 81% for Nitrofurantoin against multi drug resistant E.coli [11]. Miroslav *et al*. reported susceptibility to Fosfomycin as 95.8% against ESBL producing E.coli, and 85.3% against ESBL producing Klebsiella species [12].

Gupta *et al*. Maraki *et al*. in their study on susceptibility of various urinary tract bacteria to fosfomycin have also found no resistance to fosfomycin in E. coli [13, 14].

CONCLUSION

UTI's are the most common infections affecting all age groups. Emergence of resistant strains of pathogenic bacteria has become a major concern. In our study, most of the uropathogens including the ESBL producers showed high susceptibilities to Fosfomycin and Nitrofurantoin. Therefore their role in

empirical treatment of uncomplicated UTI's should be considered.

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