ORIGINAL ARTICLE

IN-VITRO EFFICACY OF NITROFURANTOIN, CIPROFLOXACIN AND COTRIMOXAZOLE AGAINST VARIOUS URINARY ISOLATES

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ABSTRACT

Background: Urinary tract infections are one of the most common infections especially in young adults. Due to increase in fluoroquinolones use, empirical therapy in uncomplicated urinary tract infections with this group is now controversial. This study was aimed to see the efficacy of nitrofurantoin, ciprofloxacin and cotimoxazole (trimethoprim-sulphamethaxazol); the three most common drugs which can be used orally.

Material & Methods: This descriptive study was carried out at the Department of Microbiology, Combined Military Hospital, Quetta, Pakistan from Januery 2014 to June 2014. A total of 270 urinary isolates (Outdoor 132, indoor 138) were cultured from urine specimens during the study period. Identification of isolates were performed by conventional methods and by using API 10S (Biomerieux, France). All the isolates were tested against nitrofurantoin, ciprofloxacin and cotimoxazole (trimethoprim-sulphamethaxazol) along with other routine antibiotics used for urinary pathogens.

Results: Out of total 270 urinary isolates, Escherichia coli was the dominant isolate cultured in 158 (58.51%) cases, followed by Klebsiella pneumonia in 48 (17.77%) and enterococcus spp. In 16 (5.92%) cases. Out of total 132 outdoor isolates, percentages of sensitivities of nitrofurantoin, ciprofloxacin and cotimoxazole were 92.4, 47.1 and 62.1 respectively. In case of total 138 indoor isolates, percentages of sensitivities for these three drugs were 84.0, 34.7 and 28.9 respectively.

Conclusion: Nitrofurantoin is very effective against both outdoor and indoor urinary isolates and can be used empirically for uncomplicated urinary tract infections.

Key Words: Nitrofurantoin; Ciprofloxacin; Cotimoxazole; Trimethoprim-sulphamethaxazol; Urine; Urinary Tract Infections.

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INTRODUCTION

Urinary tract infections (UTIs) are the second most common infections after respiratory tract infections.[1] According to an estimate, about 8 to 10 million people visit to clinicians for suspected UTIs.[2,3] Escherichia coli is the most common cause of UTIs both in outdoor and indoor patients. In past, ampicillin and trimethoprim-sulfamethoxazole were used as the drug of choice for treatment of uncomplicated UTIs.[4] However, their extensive used led to the development of resistance and many studies reported resistance worldwide.[5-8] Later on, quinolones became the first option for empirical treatment of UTIs. Unfortunately, due to over use and misuse of quinolones, resistance has also become a major problem in this group thus further limiting the oral antibiotic options for empirical treatment of UTIs.[9] Nitrofurantoin is effective both against gram negative and gram positive pathogens. It has less side effects, rare resistant mutants and there is no cross reactivity with other antimicrobial agents. It has given good results even against multi-drug resistant urinary pathogens.

This study was aimed to see the efficacy of nitrofurantoin, ciprofloxacin and cotimoxazole (trimethoprim-sulphamethaxazol); the three most common drugs which can be used orally.

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MATERIAL & METHODS

This laboratory based descriptive study was carried out at the Department of Microbiology, Armed Forces Institute of Pathology, Rawalpindi,

Pakistan from January 2014 to June 2014. All the urine specimens were centrifuged and those having more than 4-5 pus cells/ HPF were included in this study. No discrimination was made on the basis of age and gender. Specimens yielding growth of mixed organisms and those from urinary bag were excluded from the study. A total of 270 isolates from urine specimens were included during six months study period. In the protocol followed, all the urine samples were inoculated on CLED (Oxoid, UK) medium and incubated at 37°C for 24-48 hours. Colonies were subjected to Gram stain and rapid tests. Confirmation and species differentiation was done with traditional biochemical tests by using API 10S system (Biomerieux, France). Antimicrobial susceptibility testing was carried out on Muller Hinton Agar (Oxoid, UK) with nitrofurantoin 300µg (Oxoid, UK), trimethoprim/sulfamethoxazole 1.25/23.75µg (Oxoid, UK), ciproxin 30µg (Oxoid, UK), ampicillin 10µg (Oxoid, UK), doxycycline 30µg (Oxoid, UK), gentamicin 10µg (SPAN Diagnostic, France), ceftazidime 30µg (Oxoid, UK), tazobactem/piperacillin 10/100µg (Oxoid, UK), sulbactam/ cefoperazone 105µg (Oxoid, UK), vancomycin 30µg (Oxoid, UK), and imipenem 10µg (Oxoid, UK), by using modified Kirby-Bauer disk diffusion method.[12] Staphylococcus aureus ATCC 25923, Escherichia coli ATCC 25922 (ß-lactamase negative) and Pseudomonas aeruginosa ATCC 25853 were used as control strains.

RESULTS

Out of total 270 isolates, 132 were cultured from outdoor specimens while 138 from indoor specimens. Most of the isolates were cultured from specimens sent by gynaecological department followed by surgical department and then intensive care units. Out of total 270 isolates, 180 (67%) were from female patients while 90 (33%) were from male patients. E. coli and K. pneumonia were the dominant isolates both in indoor and outdoor specimens as shown in Table 1 and 2. Nitrofunrantoin showed maximum sensitivity both in outdoor and indoor isolates. Surprisingly, cotimoxazole showed more sensitivity as compared to ciprofloxacin in outdoor isolates as shown in Table 1 and 2. Out of 270 isolates, there were 21 (7%) which were Extended Spectrum Beta Lactamase (ESBL) producer. Out of these 21 isolates, only 2 isolates were sensitive to all the three drugs while 18 isolates were sensitive to nitrofurantion.

Table 1: Sensitivity pattern of urine samples from outdoor isolates to nitrofurantoin, ciprofloxacin and cotimoxazole (n=132)

Urinary Isolate	n	Nitro-sensitive	Cipro-sensitive	Cotimoxazole-sensitive
E. coli	90	86	41	53
K. pneumoniae	24	20	14	18
A. johnsonnii	4	4	2	3
Enterococcus spp.	4	3	1	2
Proteus spp.	2	2	1	1
S. odorifera	2	2	1	1
Staph aureus	2	2	1	2
Salmonella typhi	2	2	1	2
Pseudomonas	2	2	1	0

Table 2: Sensitivity pattern of urine samples from indoor isolates to nitrofurantoin, ciprofloxacin and cotimoxazole (n=138)

Urinary Isolate	n	Nitro-sensitive	Cipro-sensitive	Cotimoxazole-sensitive
E. coli	68	60	21	18
K. pneumoniae	24	18	10	5
Pseudomonas	14	8	6	3
A.baumannii	12	8	4	7
Enterococcus	12	8	3	4
Serretia spp.	6	4	3	2
Proteus spp.	2	1	1	1

DISCUSSION

In recent years, the treatment of UTIs has become difficult due to increase in the resistance rates of commonly used antibiotics.[10] Treatment of UTIs with fluorquinolones may not be fruitful due to increase use of this class of antibiotics empirically. In our setup, fever is also treated with ciprofloxacin without confirmation of salmonella thus further increasing resistance. In one of the study, survey showed that 100 patients suspected of having UTI were given fluoroquinolones and out of them 81 were given inappropriate treatment.[11] Nitrofurantoin has emerged as the return of an old friend in the wake of growing resistance.[12] Various studies done throughout the world on the efficacy of nitrofurantoin showed that its resistance is still low and it can be used safely as an empirical therapy for uncomplicated UTIs.[13,14] However, its use is still controversial in some countries such as Germany due to its serious but rare side effects such as polyneuropathy and interstitial pneumonia. Due to the disuse of cotimoxazole, it was postulated that its resistance rate might have decreased with the passage of time.

In our study, E.coli was the predominant isolate (58%) and overall susceptibility of E.coli to nitrofurantoin, ciprofloxacin and cotimoxazole was 92.4%, 39.2% and 44.9% respectively. The results of our study clearly show that nitrofurantoin is most effective drug against E.coli both in outdoor (95.5%) and indoor (88.2%) patients. The difference in the susceptibilities of nitrofurantoin against E.coli in outdoor and indoor isolates is significant ($p < 0.001$). The results of our study are comparable to a study done by Tekin et al.[10] In this study, the overall susceptibility of nitrofurantoin for outdoor and indoor isolates was 93.1 and 89.2%. Another interesting observation in our study was that cotimoxazole is more effective as compared to ciprofloxacin against E.coli in outdoor patients while it is less effective as compared to ciprofloxacin in indoor E.coli isolates. In another study done at USA in 2008, the susceptibility of nitrofurantoin, ciprofloxacin and cotimoxazole against E.coli was 96, 75, and 80% respectively thus clearly proving that cotimoxazole is more effective in-vitro than ciprofloxacin against E.coli.[12]

Klebsiella pneumonia was the second most common organism isolated both from outdoor and indoor specimens (17.7%) out of total 270 isolates. Overall susceptibility of K. pneumonia to nitrufurantoin, ciprofloxacin and cotimoxazole was 79.1%, 50.0% and 47.9% respectively. Susceptibility of K. pneumonia to nitrofurantoin for outdoor and indoor isolates was 83.3% and 75%. These results suggest that nitrofurantoin has fairly good activity against K. pneumonia isolates which is the second most common cause of UTIs.

Acinetobacter baumannii was a big problem in our study especially in hospitalized patients. Out of total 270 isolates, 12 (4.4%) were Acinetobacter baumannii and majority of them were multi-drug resistant. This might be due to the spread/transfer of MDR isolates from ICUs to wards due to poor infection control practices. Out of total twelve A. baumannii isolates, the susceptibility pattern of these isolates against nitrofurantoin, ciprofloxacin and cotimoxazole was 66.0%, 33.3% and 58.3%. Our local data showed that A. baumanni isolated from ventilator and catheterized patients showed very good sensitivity to less commonly used and low cost antibiotics such as cotimoxazole and doxycycline. Among the A. baumanni isolates cultured from ventilator patients, doxycycline or cotimoxazole was the only option along with polymyxin. A study done by Pour et al in India showed that most of the A. baumannii isolates cultured from catheterized patients form biofilms in the catheter thus posing a serious therapeutic challenge and the only option left is to remove the indwelling catheter.

CONCLUSION

Nitrofurantoin is very effective against both outdoor and indoor urinary isolates and can be used empirically for uncomplicated urinary tract infections.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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None declared.