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Study of Nitrofurantoin Susceptibility in Bacterial Isolates from Patient of Urinary Tract Infection Attending Tertiary Care Centre

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A B S T R A C T

Increasing resistance rates of bacteria against standard antibiotics has become great problem for the treatment of UTI. To fight with this problem, an old drug Nitrofurantoin getting good attraction. Action at multiple sites and achieving levels in urine is the major strength of Nitrofurantoin as well as tolerated orally well and Side-effects are very less. Methodology: Study was conducted in Microbiology Department from April 2016 to April 2017. Urine samples were collected from patient admitted in various wards and attending O.P.D. and transport to laboratory. Every urine specimen received in the Microbiology laboratory was processed according to the recommended procedures for the isolation and identification of bacterial isolates. Bacteria were identified by colony morphology, gram staining and biochemical test from the primary isolation plates. Antibiotic susceptibility testing done for each isolates by DDT of Kirby Bauer on Muller Hinton Agar according to CLSI guideline. 357 urinary isolates were recovered with significant count in study period. *E. coli* 213 (59.66%) was the commonest organism isolated followed by *Klebsiella pneumoniae* 46 (12.89%), *Enterococcus* spp 33 (9.24%). Nitrofurantoin susceptibility in our study for *E. coli* was 72.3%, *Klebsiella* spp. 30.6%, *Enterococcus* 69.71%, *Staphylococcus aureus* 85.71%, *Enterobacter* 60 % and CONS 100%. However Mariraj *et al.*, (2016) found 80-90% susceptibility for all urinary isolates and Rajesh *et al.*, (2010) found *E. coli* was 82%, *Klebsiella* spp. 92 %, *Enterococcus* 00.00%. In the present era of antibiotic resistance urinary isolates show very good susceptibility for nitrofurantoin as compare to other commonly use antibiotic for treatment.

Introduction

Urinary tract Infections are among the most common infectious diseases in humans.[1] the source of organisms producing UTI is the flora of Intestine tract.[2, 3, 4] Non-judicial use of antibiotic therapy lead to resistance in the flora of intestinal bacteria.[3] this will also lead to spread of antimicrobial resistance among bacteria.[5]

Increasing resistance rates of bacteria against standard antibiotics has become great problem for the treatment of UTI (Alicem Tekin *et al.*, 2012). To fight with this problem, an old drug Nitrofurantoin getting good attraction. >50 years extensive use worldwide on uropathogens, there has been virtually no acquired resistance to Nitrofurantoin (Rizvi *et al.*, 2011).

Action at multiple sites and achieving levels in urine is the major strength of Nitrofurantoin. This include inhibition of bacterial enzymes involved in carbohydrate synthesis and blocking of DNA, RNA, and total protein synthesis in higher concentration.[6,7] Nitrofurantoin is metabolized in renal tissue and rapidly excreted in the urine. Due to this rapid excretion, the urinary concentration of nitrofurantoin is more than 100 µg/mL (up to 250 µg/mL).

This higher concentration in urine makes it an ideal choice for treatment of urinary tract infection (UTI). Nitrofurantoin is usually well tolerated orally. Side-effects occur are very less.[8] Macrocrystal formulations used to reduce gastrointestinal side effects such as nausea and vomiting.

In glucose-6-phosphate deficiency patients Haemolytic anaemia can occur. But serious adverse effects are rare and can be seen only with prolonged medication (>6 months).[6] these includes chronic pulmonary reactions, interstitial fibrosis, peripheral neuropathy and hepatic injury. Nitrofurantoin can be given safely in pregnancy (pregnancy category B).[9]

Nitrofurantoin cannot use in patients with renal failure with creatinine clearance rate of 60 mL/min. However, some recent studies indicate its use can be expanded to creatinine clearance as low as 40 mL/min.[10]

The main aim and objectives of present study is to determine the susceptibility of Nitrofurantoin in the isolates recovered from patients with significant bacteriuria, Isolation and Speciation of bacteria and to determine the antimicrobial susceptibility profile.

Inclusion criteria

All urine specimens having bacterial growth of all age group.

Exclusion criteria

All urine specimens not having bacterial growth.

All urinary isolates for which Nitrofurantoin susceptibility not recommended by CLSI[13]

Materials and Methods

Study was conducted in Microbiology Department from April 2016 to April 2017. Urine samples were collected from patient admitted in various wards as well as patient attending O.P.D. and transport to laboratory.[11]

Every urine specimen received in the Microbiology laboratory was processed according to the recommended procedures for the isolation and identification of bacterial isolates.[11]

Bacteria was identified by colony morphology, gram staining, biochemical test from the primary isolation plates.[11]

Antibiotic susceptibility testing done for each isolates by DDT of Kirby Bauer on Muller Hinton Agar according to CLSI guideline.[12]

Results and Discussion

357 urinary isolates were recovered with significant count in study period. *E. coli* 213 (59.66%) was the commonest organism isolated followed by *Klebsiella pneumoniae* 46 (12.89%), *Enterococcus spp* 33 *(*9.24*%),* *Pseudomonas spp*. 20 (5.60%), *S. aureus* 14 (3.92%), *Enterobacter* 10 (2.8%), *Citrobacter spp.* 6(1.68%), *Acinetobacter baumannii* 5 (1.4%), *Klebsiella oxytoca* 3 (0.84%), Coagulase negative Staphylococcus 3 (0.84%), *Proteus mirabilis* 3 (0.84%) and *Providencia rettgeri* 1 (0.28%). *Pseudomonas spp*., *Acinetobacter baumannii*, *Proteus mirabilis* and *Providencia rettgeri* were

excluded from our study due to Nitrofurantoin susceptibility not recommended by CLSI[13].

Most susceptible antibiotic for *E. coli* was Nitrofurantoin 72.3% followed by Carbapenams 69.48% and Amikacin 63.85%. Klebsiella pneumoniae showing susceptibility for Carbapenams 50%, Amikacin 43.48%, Piperacillin-Tazobactum 41.3%, Nitrofurantoin 30.43%.

Susceptibility of Nitrofurantoin for Enterococcus 69.7% just after Linezolid, Teicoplanin and Vancomycin. In Staphyloccus aureus Susceptibility of Nitrofurantoin become equal to Linezolid, Vancomycin i.e. 85.71%. Highest susceptibility for Nitrofurantoin also shown in *Citrobacter* spp. (60%) (Also see tables 1 and 2; chart 1).

E. coli was the commonest organism isolated in our study followed by *Klebsiella pneumonia* and *Enterococcus spp., Pseudomonas spp*., *S. aureus*, *Enterobacter spp., Citrobacter spp., Acinetobacter baumannii*, *Klebsiella oxytoca*, Coagulase negative Staphylococcus, *Proteus mirabilis* and *Providencia rettgeri*. Mariraj *et al.,* (2016) and Rajesh *et al.,* (2010) also report *E. coli* as a commonest organism followed by *Klebsiella spp., Enterococcus spp, Pseudomonas spp*., *S. aureus* in their study.

Resistant pattern in urinary isolates were high in our study. Mariraj *et al.,* (2016) and Rajesh *et al.,* (2010) also report high resistance in their study. In this study, the treatment option is either injectable and/ or costly antibiotics for the treatment of urinary tract infection. In such scenario Nitrofurantoin is an orally available and cost effective good alternative.

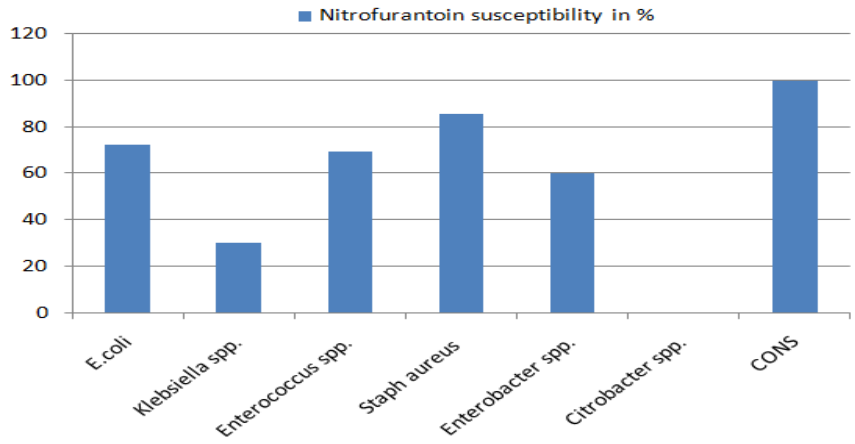
Table.1 Distribution of antimicrobial susceptibility for gram negative urinary isolates

Antibiotics	***E. coli* (n=213)**	***Klebsiella pneumoniae* (n=46)**	***Klebsiella oxytoca* (n=3)**	***Enterobacter spp.* (n=10)**	***Citrobacter* (n=6)**
Ampicillin	5 (2.35%)	3 (6.52%)	0	0	0
Amoxycillin-clavunate	23 (10.80%)	4 (8.70%)	0	0	0
Piperacillin	27 (12.68%)	7 (15.22%)	0	3 (30%)	0
Cefotaxime	29 (13.62%)	7 (15.22%)	0	1 (10%)	0
Ceftriaxone	32 (15.02%)	9 (19.57%)	0	2 (20%)	0
Cefepime	33 (15.49%)	9 (19.57%)	0	0	0
Piperacillin- Tazobactum	114 (53.52%)	19 (41.30%)	0	4 (40%)	0
Ticarcillin-Clavunate	24 (11.27%)	6 (13.04%)	0	1 (10%)	0
Ampicillin-Sulbactum	65 (30.52%)	15 (32.61%)	0	3 (30%)	0
Amikacin	136 (63.85%)	20 (43.48%)	1 (33.33%)	4 (40%)	0
Gentamicin	109 (51.17%)	15 (32.61%)	0	3 (30%)	0
Cotrimoxazole	48 (22.54%)	12 (26.09%)	1 (33.33%)	2 (20%)	1 (16.67%)
Ciprofloxacin	28 (13.15%)	11 (23.91%)	0	2 (20%)	0
Imipenem	148 (69.48%)	23 (50.00%)	2 (66.67%)	4 (40%)	0
Meropenem	148 (69.48%)	23 (50.00%)	2 (66.67%)	4 (40%)	0
Ertapenem	148 (69.48%)	23 (50.00%)	2 (66.67%)	4 (40%)	0
Nitrofurantoin	154 (72.30%)	14 (30.43%)	1 (33.33%)	6 (60%)	0
Norfloxacin	30 (14.08%)	10 (21.74%)	0	1 (10%)	0
Nalidixic acid	14 (6.57%)	6 (13.04%)	0	0	0

Table.2 Distribution of antimicrobial susceptibility for Gram positive urinary isolates

Antibiotics	*Staphylococcus aureus* (n=14)	Coagulage Negative *Staphylococcus* (n=3)	*Enterococcus* spp. (N=33)
Ampicillin	2 (14.29%)	0	9 (27.2%)
Amoxycillin-clavunate	3 (21.43%)	2 (66.67%)	-
Amikacin	12 (85.71%)	3 (100%)	-
Gentamicin	9 (64.29%)	3 (100%)	-
Cotrimoxazole	7 (50.00%)	1(33.33%)	-
Ciprofloxacin	4 (28.57%)	0	2 (6.06%)
Nitrofurantoin	12 (85.71%)	3 (100.00%)	23(69.7%)
Norfloxacin	3 (21.43%)	1(33.33%)	1 (3.03%)
Nalidixic acid	1 (7.14%)	0	0
Penicillin-G	1 (7.14%)	0	0
Oxacilline	4 (28.57%)	2 (66.67%)	-
Cefazoline	1 (7.14%)	0	-
Chloramphenicol	8 (57.14%)	2 (66.67%)	-
Erythromycin	5 (35.71%)	1(33.33%)	-
Clindamycin	7 (50.00%)	2 (66.67%)	-
Tetracyclline	6 (42.86%)	1(33.33%)	3 (9.09%)
Teicoplanin	14 (100.00%)	3 (100.00%)	28(84.8%)
Linezolid	12 (85.71%)	3 (100.00%)	33(100%)
High Level Gentamicin	-	-	7 (21.2%)
Vancomycin	-	-	27(81.8%)

Chart.1 Showing distribution of nitrofurantoin susceptibility for urinary isolates



Nitrofurantoin susceptibility in our study for *E. coli* was 72.3%, *Klebsiella* spp. 30.6%, Enterococcus 69.71%, *Staphylococcus aureus* 85.71%, *Enterobacter* 60 % and CONS 100%. However, Mariraj *et al.*, (2016) found 80-90% susceptibility for all urinay isolates and Rajesh (2010) found *E. coli* was 82%, *Klebsiella* spp. 92 %, *Enterococcus* 00.00% (Chart 1). In the present era of antibiotic resistance urinary isolates show very good susceptibility for nitrofurantoin as compare to other commonly use antibiotic for treatment. Amikacin, Carbapenams, Piperacillin-Tazobactum for gram negative and Vancomycin and Linezolid

are also a good option in spite of emerging of highly resistant strain worldwide, but on the basis of pharmokinetic and dynamic Nitrofurantoin is the better option. Similarly for UTI in pregnancy nitrofurantoin is safe and effective option.

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