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Nitrofurantoin Resistance Among Common Urinary Isolates in Uncomplicated Urinary Tract Infection

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Abstract: *Despite being a common health problem, community acquired uncomplicated Urinary Tract Infection (UTI) is a bit under- rated because of its lower mortality rate, relative ease of diagnosis and easily available oral remedy for it. But ever increasing antibiotic –resistance of the uropathogens has forced us to have another look into this matter. This study is an effort to see whether the less commonly prescribed oral antibiotic like Nitrofurantoin can be a better option for treatment before switching over to the final option of intravenous antibiotic therapy.Mid-stream urine samples were collected from 642 symptomatic UTI patients, out of which, 111 were culture positive. The predominant organism was Escherichia coli, CONS, S. aureus, Klebsiella species. Very high level of resistance was observed against fluoroquinolones, ampicillin, amoxycillin –clavulanic acid, cephalosporins. But, Nitrofuranrtoin resistance was relatively less-21%. The other antibiotics which showed equal or higher level of susceptibility than Nitrofurantion were all injectable preparations-Imipenem, Cefoperazone-sulbactam, Amikacin and Gentamicin. So, in the current scenario, use of Nitrofutantion to treat uncomplicated community acquired UTI should be considered in our state.*

Keywords: *Community acquired UTI, Nitrofurantion resistance, Urinary tract infection, UTI*

I. Introduction

Community acquired urinary tract infection (UTI), although a common infection, enjoys a lesser importance due to the following perceptions- lower mortality rate of uncomplicated UTI, relative ease of diagnosis by simple mid- stream urine culture and ease of treatment by simple short course chemotherapy.

Nevertheless, data of increased prevalence, cost, morbidity, antibiotic resistance, recurrence and relapse suggest that clinician should have another look to community acquired uncomplicated UTI.[1]

Typically there are fewer and fewer oral antibiotic choices, and the question is: What compounds might we have at hand to use, or do we need to resort to intravenous antibiotic therapy? This is an increasingly frequent problem. David Livermore has published a nice series on Klebsiella pneumoniae carbapenemase (KPC) organisms and found that less than a quarter of them are still susceptible to either ciprofloxacin, chloramphenicol, or nitrofurantoin.[2]

II. Materials And Methods

Mid –stream urine specimens were collected from patients presenting with clinical symptoms of urinary tract infections. Urine specimens were inoculated in MacConkey's agar and CLED agar following standard protocol. The isolates were identified by the sets of standard biochemical reactions i.e. Indole production, MR reaction, VP test, Citrate utilisation, Urease production, sugar fermentation reactions and other phenotypic methods. Antibiotic sensitivity was done by Kirby- Bauer method on Mϋller Hinton agar plate. The results were analysed and interpreted as standard CLSI guidelines.

III. Result And Analysis

Altogether 642 patients with suspected urinary tract infection were included in this study. Mid-stream urine specimens were collected from them using standard collection technique. 111 were culture positive. The microbial profile of the culture positive urine was predominated by Escherichia coli, followed by Coagulase negative Staphylococcus Species (CONS), Staphylococcus aureus, Enterococcus faecalis, and Klebsiella species. Several other species were also involved like Proteus vulgaris and Proteus mirabilis, Citrobactor species, Pseudomonas species, and Serratia sp.(in one case).

Antibiogram of the isolates showed varied degree of resistance. Nitrofurantion (NFT) resistance was seen in 24 isolates(21.62%). 8 E. coli, 5 Klebsiella sp.,5 Enterococcus sp., 2 CONS, and one each for S. aureus, Proteus sp., Citrobactor sp., and Pseudomonas Sp. were NFT resistant. Majority of the isolates were mostly sensitive to nitrofurantoin, whereas, resistant to most of the commonly employed antibiotics for UTI.

IV. Figures and tables

Table: 1. Bacteriological profile of UTI (n=111)

Organism	Number	Percentage
E. coli	42	37.84
CONS.	16	14.41
S. aureus	14	12.61
Klebsiella species	13	11.71
Enterococcus Sp.	13	11.71
Pseudomonas sp.	5	4.50
Proteus sp	2	1.80
Citrobactor sp.	5	4.50
Serratia sp.	1	0.90

Table 2: antibiotic sensitivity pattern of the isolates against commonly used antibiotics

Anti-biotics	E. coli 42	CONS 16	S. aureus 14	Klebsiella sp. 13	Entero Coccus Sp. 13	Proteus sp. 2	Citro bactor sp. 5	Pseudo monas sp. 5
Amc								
S	4	12	8	2	4	1	3	1
R	38	4	6	11	9	1	2	4
Ak								
S	35	14	12	7	10	1	4	3
R	7	2	2	6	3	1	1	2
Gm								
S	34	14	10	4	10	1	3	2
R	8	2	4	7	3	1	2	3
Ctx								
S	6	11	8	2	9	1	0	0
R	36	5	6	11	4	1	5	5
Nit								
S	34	14	13	8	8	1	4	4
R	8	2	1	5	5	1	1	1
Imp								
S	40	-	-	10	-	2	5	4
R	2			3		0	0	1
Cip								
S	4	11	5	0	1	0	1	0
R	38	5	9	13	12	2	4	5
le								
S	5	11	6	1	1	0	2	0
R	37	5	8	12	12	2	3	5
Pit								
S	5	12	6	6	7	1	2	1
R	37	4	8	7	6	1	3	4
Cfs								
S	20	12	7	7	13	2	4	1
R	22	4	7	6	0	0	1	4

Table 3: Prevalence of NFT resistance among the bacterial isolates- (n=111)

Organism	Number	NFT sensitive (%)	NFT resistant (%)
E. coli	42	34 (80.95)	8 (19.04)
CONS	16	14 (87.5)	2(12.5)
S. aureus	14	13 (92.85)	1(7.1)
Klebsiella sp.	13	8 (61.54)	5(38.46)
Enterococcus Sp.	13	8 (61.54)	5(38.46)
Proteus sp.	2	1 (50)	1(50)
Citrobactor sp.	5	4 (80)	1(20)
Pseudomonas sp.	5	4 (80)	1(20)
Serratia sp.	1	1 (100)	0

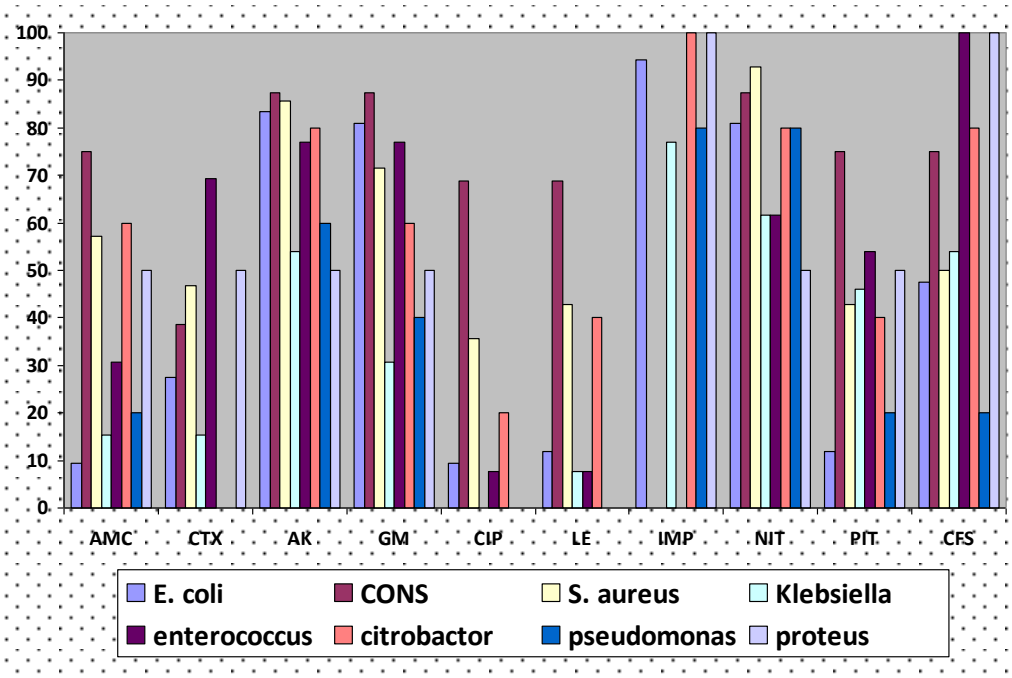

Figure 1: sensitivity pattern (in percentage) of common urinary isolates against commonly used antibiotics

IV. Discussion

Urinary tract infections (UTI) are common infections in both community and hospital set up. Treatment of UTI varies with the type of involvement –upper or lower UTI, type of organism, as well as age, sex and underlying disease of the patient. [2] The aetiology of UTIs is predictable with Escherichia coli being the principal pathogen.[3] other common isolates were Klebsiella species, coagulase negative Staphylococcus, Staphylococcus aureus, Enterococcus species. The rate of isolation of other gram negative uropathogens was relatively less in our study in comparison to the 'urinary tract infection study group' in Turkey lead by Arslan et al in 2004. [4] The most commonly used antibacterial drugs in the treatment of community-acquired UTIs are Trimethoprim/sulfamethoxazole, ciprofloxacin, cephalosporins, semi-synthetic penicillins with or without inhibitors, nitrofurantoin and fosfomycin.[6] In treatment of UTIs, trimethoprim/ sulfamethoxazole is the recommended drug in settings where the prevalence of resistance is <10–20% according to the Infectious Diseases Society of America (IDSA) guidelines.[2] Fluoroquinolones are the drugs of choice if the trimethoprim/sulfamethoxazole resistance rate is higher than 20%.[2] Fluoroquinolones are potent antimicrobials, have been in clinical use for the last two decades,[6] and have been more commonly prescribed for community-acquired UTIs, although there is evidences of increasing fluoroquinolones resistance worldwide. An association between the increase in quinolone prescriptions and an increase in bacterial resistance has been reported from several different countries.[6–9]

In this study, fluoroquinolone resistance of E. coli was found to be more than 80%. A high level of resistance was observed for beta-lactam antibiotics, and beta lactam-beta lactamase inhibitors combination drugs. But in vitro susceptibility to nitrofurantion was quite high (80.95%). This report goes in harmony with the report of Giancarlo Schito, MD, (Italy), who presented an epidemiological and surveillance study involving 9 countries. Their study found that for E.coli isolates susceptibility was highest for fosfomycin (98.4%), followed by mecillinam (95.9%), nitrofurantoin (95.2%), ciprofloxacin (91.2%), amoxicillin/clavulanic acid (82.6%), cefuroxime (80.9%), cotrimoxazole (71.1%), and lowest for ampicillin (45.0%). Fosfomycin, mecillinam, and nitrofurantoin have preserved their overall in vitro efficacy.[10] According to these patterns of E. coli prevalence and resistance, ampicillin, cotrimoxazole, and cefuroxime should not be recommended for empiric therapy of UTI in all countries monitored. The increase in quinolone resistance among community-acquired urinary E. coli is a cause of concern. In a study (in 2004) by Hooton, Besser and Foxman, Nitrofurantoin was recommended for treating or preventing only uncomplicated cystitis and resistance to E. coli has been reported to be very low even after 50 years of use. [11]

V. Conclusion

Various studies showed that empirical therapy of community acquired uncomplicated UTI with fluoroquinolones or beta lactam antibiotics may be less effective due to higher rates of resistance, whereas nitrofurantion may be a reasonable alternative due to much lower rate of resistance. Though nitrofurantion

resistance is also increasing and the data in our study is higher than some previous studies, it is still lower than the other antibiotics so it's role in treating the patients with uncomplicated UTI should be considered again. [8,11,12,13,14]

This study has not touched the sensitive topic of complicated UTI in individuals with low Glomerular filtration Rate (GFR), which rules out nitrofurantoin, tetracycline and Sulfa compounds. Yes, this is a difficult time.

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