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An observational study to evaluate the Antimicrobial prescribing pattern in urinary tract infection

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Abstract

Background: Urinary tract infection (UTI) is a common illness affecting both males and females in almost all age groups. Varieties of antimicrobials such as cotrimoxazole, nitrofurantoin, fluoroquinolones, and penicillin are effective for treatment of UTI. **Aims and Objectives:** The present observational study was planned to generate data on antimicrobial use pattern in UTI which could be beneficial in selection of rational drug therapy in UTI. **Materials and Methods:** The study was carried out by analyzing indoor and outpatient department case records of UTI patients of a tertiary care hospital. The demographic data and prescription pattern, urine culture report, along with the antimicrobial sensitivity testing were evaluated. The data were analyzed by routine descriptive statistics. **Results:** *Escherichia coli* was the most common organism to be isolated in urine culture followed by *Staphylococcus aureus*. Cephalosporin group was the most prescribed antibiotics in all age groups. Although nitrofurantoin and cotrimoxazole were showing good sensitivity pattern when compared with other antimicrobial groups, these were least prescribed. **Conclusion:** The choice of antimicrobial drugs should be individualized based on patient compliance, adverse effects, availability and costing factors, along with prevailing sensitivity pattern in the locality. Nitrofurantoin can be better alternative for uncomplicated UTI when compared to third generation cephalosporins.
Keywords: Antimicrobial; Cephalosporins; Drug Resistance; Nitrofurantoin; Urinary Tract Infection

Introduction

Urinary tract infection (UTI) is a common and painful illness accounting for 1-3% consultations in general medical practice and mostly responding to antibiotic therapy.[1] It consists of variety of clinical diseases such as asymptomatic bacteriuria (ABU), cystitis, prostatitis, and pyelonephritis.[2] In ABU, there is the absence of symptoms attributable to the bacteria in the urinary tract, and the patient does not usually seek treatment, while UTI is symptomatic and the patient presents to the clinician for antimicrobial therapy.[3] UTI occurs more commonly in females than in males. As many as 50-80% of women in the general population acquire at least one UTI during their lifetime because of short urethra and its proximity to vagina which acts as a reserver of microorganisms.[4,5] Acute uncomplicated cystitis may recur in 27-44% of healthy women, even though they have normal urinary tract.[6] A variety of uropathogens is involved mainly aerobic Gram-negative bacilli such as *Escherichia coli*, *Klebsiella*, *Proteus*, *Citrobacter*, *Acinetobacter*, *Morganella*, and *Pseudomonas aeruginosa*. Gram-positive bacteria such as *Staphylococcus aureus, Staphylococcus saprophyticus*, *Enterococci* and yeasts are also important pathogens in complicated UTI. Candida infection may be a complication in case of catheterization and in patients in ICU or in immune-compromised

state. Detection of bacteria in urine culture and its sensitivity testing is the diagnostic "gold standard" for UTI. However, culture results take at least 24-48 h after the patient's sample is received.Antimicrobial therapy is needed for any symptomatic UTI. The choice of antimicrobial agent and the dose and duration of therapy depend on the site of infection, presence or absence of complicating conditions and on local resistance pattern.[2] First-line agents include trimethoprim-sulfamethoxazole and nitrofurantoin which are mostly used in uncomplicated UTI. Second-line agents include fluoroquinolones and β-lactam compounds. Fluoroquinolones such as ofloxacin, ciprofloxacin, and levofloxacin are highly effective for short- course therapy for cystitis. Moxifloxacin is not recommended for UTI as it does not achieve adequate urinary levels. Except for pivmecillinam, rates of pathogen eradication are lower and relapse rates higher with β-lactam drugs as they fail to eradicate uropathogens from the vaginal reservoir.[2] Fosfomycin may be effective in UTI caused by multi-drug resistant *E. coli*.Hence, it is a huge challenge for selecting appropriate antimicrobial agents for the treatment of UTI due to lack of proper surveillance mechanisms for monitoring antimicrobial use. Dearth of microbiology laboratory support adds to the challenge.[7] Moreover, the nature and pattern of antimicrobial prescribing practice changes with time as spectrum of pathogens change and new antimicrobials are introduced. Hence, a drug use study can help in reviewing irrational and unnecessary prescribing pattern, which acts as huge financial and physical burden to patient. With this background, the present observational study was planned in medicine ward of our tertiary care hospital to find out the

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antimicrobial use pattern in UTI along with common organisms causing it and correlating it with urine culture and sensitivity study to generate data on antimicrobial use pattern in UTI which could be beneficial in selection of rational drug therapy in UTI.

Materials and Methods

The present study was conducted at Department of Pharmacology, at Vardhman Institute of Medical Sciences, Pawapuri. The study was approved by institutional research and ethical research committee. Informed consent was taken from all the participants after explaining the study protocol. The study was conducted over a period from March 2018 to September 2019.The study sample consisted of both outpatient department (OPD) and indoor admission records (from) of patients admitted with a diagnosis of UTI at our institute. Inclusion criteria included cases with provisional diagnosis of UTI with supportive laboratory investigation reports like urine pus cell positive, with or without urine culture positive. For Indoor patients, case sheets were collected from the medical records department based on disease coding. And for OPD patients, scanned copies of prescriptions of Medicine Department obtained from record room were evaluated. Confidentiality of patient information was properly ensured using code numbers in place of patient's personal identification. The demographic data and prescription pattern of each case sheet were thoroughly evaluated. The relevant investigations (microbiological and hematological) were noted down with the urine culture report if available along with the antimicrobial sensitivity testing. Different antibiotics used to treat the UTI along with their dose, frequency and duration of treatment was recorded. [8] All the laboratory investigation with special importance to urine culture report with antimicrobial sensitivity pattern was thoroughly evaluated. Condition of the patient at the time of discharge was also noted. The data were entered and summarized in Microsoft Excel worksheet version 2009, and routine descriptive statistics were used for analysis. All data were expressed as percentages for categorical variables.

Results

During the study period, case records and OPD prescriptions of 269 patients of medicine department were analyzed. Out of these, 43 cases were excluded from the study as they were having other coexisting illnesses such as malaria and typhoid fever. 34 cases were excluded as they were not having supportive laboratory investigation reports suggesting UTI. Among these 192 (123 indoor admission and 69 OPD cases), 43 were males and 149 were females. The age wise distribution of UTI patients summarized in Table 1 which indicates that the overall incidence in female is more than that in males in all age groups.

Table 1: Demographic data of patients admitted with UTI

Age	Sex	Frequency (%)	Total=192 (%)
10-20	Male	8 (28.5)	28 (14.6)
	Female	20 (74.5)	
21-40	Male	11 (17)	64 (33.4)
	Female	53 (82)	
41-60	Male	12 (12)	59 (30.7)
	Female	47 (79)	
>60	Male	16 (39)	41 (21.3)
	Female	25 (61)	
UTI: Urinary tract infection			

After the age of 60, the incidence in males and females is almost equal due to increased cases of UTI in males because of obstructive uropathy from prostatic hypertrophy. Over the study period, the total number of antimicrobial agents prescribed to the 192 UTI cases was 257. Table 2 provides a consolidated data of broad group of antimicrobials used.

Table 2: Percentage of distribution of different antimicrobials.

Antibiotic class	Individual antibiotics prescribed	Number of patients	Total (%)
Cephalosporin	Cefritriaxone	84	155 (60.3)
	Cefritriaxone+sulbactam	18	
	Cefoperazone	13	
	Cefotaxime	5	
	Ceftazidime	3	
	Cefixime (oral)	32	
Fluoroquinolines	Ofloxacin (oral)	14	41 (16)
	Ofloxacin (IV)	20	
	Ciprofloxacin	4	
	Prulifloxacin	3	
Penicillins	Amoxicillin+clavulanic acid	5	26 (10)
	Piperacillin+tazobactam	21	
Monobactams	Aztreonam	3	3 (1.17)
Carbapenems	Meropenem	6	6 (2.3)
Macrolide	Azithromycin	4	7 (2.7)
	Clarithromycin	3	
Oxazolidinone	Linezolid	3	3 (1.16)
Aminoglycosides	Amikacin	5	5 (1.95)
Glycopeptide	Vancomycin	2	2 (0.8)
Nitroimidazole	Metronidazole	5	5 (1.95)
Urinary antiseptics	Nitrofurantoin	4	4 (1.55)

As evident from this data, the highest number of antimicrobial prescriptions were from the cephalosporins (60.3%), followed by fluoroquinolones (15.95%) and penicillins (10.11%). Among the injectable cephalosporins, the highest prescribed was ceftriaxone with or without sulbactam, followed by cefoperazone and cefotaxime. Oral cefixime was prescribed in 32 cases. Quinolones constituting ciprofloxacin, ofloxacin, and prulifloxacin account for the second highest number of prescriptions. Other β-lactams,

macrolides, aminoglycosides, vancomycin, etc., together accounted for 15% prescriptions. In 40% cases, treatment was guided by urine culture and sensitivity report. In most cases (60%), antimicrobial therapy was empirical and based on clinical judgment.While analyzing urine culture and sensitivity report, it was observed that out of the 136 cases of urine culture positive, *E. coli* was isolated in 82 cases, followed by *S. aureus* in 18 cases. *Klebsiella, P. aeruginosa*, and *Enterococcus* accounted for 16, 6, and 6 cases, respectively. *Candida albicans* was isolated in 8 cases. Out of these two common organisms, *E. coli* (Gram-negative) and *S. aureus* (Gram-positive) were selected for antibiotic sensitivity study. The antibiotic sensitive and resistance pattern in case of *E. coli* and *S. aureus*, the two most common isolated microorganisms in urine culture. *E. coli* and *S. aureus* are mostly resistant to third generation of cephalosporins, the most commonly prescribed antibiotic, but are showing good sensitivity to aminoglycosides such as gentamicin and amikacin. But surprisingly, nitrofurantoin and cotrimoxazole which are showing good antimicrobial activity against most organisms are least prescribed.

Discussion

The study was carried out in a tertiary care hospital by analyzing OPD prescription and indoor case records of the patient of UTI. 257 antimicrobial agents were prescribed in 192 UTI patients. Cephalosporins were most commonly used followed by fluoroquinolones and penicillins. Analysis of urine culture and sensitivity report shows *E. coli* was the most common microorganism isolated, followed by *S. aureus*. In antibiotic sensitivity test, both these microorganisms were mostly resistant to third generation of cephalosporins, the most commonly prescribed antibiotic but showed good sensitivity to gentamicin, amikacin, nitrofurantoin, and cotrimoxazole.Our study results corroborate with the study of Pargavi et al.,[9] who have also found *E. coli* to be the most commonly isolated organism in urine culture and with Bay and Anacleto,[10] who had observed that cephalosporins were the most common antimicrobial used in UTI. According to Gupta et al.,[11] nitrofurantoin is a well-tolerated drug and has good efficacy when given twice daily for 5 days and it has a low propensity for ecological adverse effects.Study result may be limited by the fact that, initial antibiotic treatment received by the UTI patients before coming this hospital and its effect on urine culture sensitivity test was not taken into consideration. Since this is a tertiary care hospital dealing with patients mostly referred from primary and secondary health center; prescribers may be preferring second and third line drugs over first line drugs, which may be one of the reasons behind low use of nitrofurantoin and cotrimoxazole.

Conclusion

The study highlights the disease pattern in adult and geriatric population along with prescribing pattern of antibiotics in UTI. It also gives us some idea about common organisms responsible for UTI, along with their drug sensitivity. Therapeutic approach for UTI is initially empirical as there is delay in getting culture report. Third generation cephalosporins are the most commonly used as it covers both Gram-positive and Gram-negative organisms. But as per observation, the most common causative organisms such as *E. coli*

and *S. aureus* mostly show resistance to them. Nitrofurantoin and cotrimoxazole least commonly prescribed drug showing good activity against these organisms. Hence, new uncomplicated cases can be initially prescribed with orally effective first line drugs and keeping the injectable second and third line drugs for complicated UTI and indoor admission cases. The choice of antimicrobial drugs should be individualized based on patient compliance, adverse effects, availability and costing factors, along with sensitivity pattern in the locality. Whenever culture report is available, therapy should be according to the sensitivity report. Periodic review of antibiotic sensitivity should be done to modify the empirical treatment of UTI.

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