ORIGINAL ARTICLE

DRUG UTILIZATION STUDY ON ANTIMICROBIAL USE IN URINARY TRACT INFECTION

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ABSTRACT

Introduction: Antimicrobials are prescribed commonly for urinary tract infection. But if not used rationally then there will be increase chances of resistance of bacteria as well as increase in duration of morbidity and total cost of therapy. This study was conducted to throw light the antimicrobial utilization pattern.

Aim: To study and analyze the pattern of antimicrobial utilization in UTI.

Method: A descriptive retrospective study was conducted in tertiary care hospital for 6 months. Case sheets diagnosed with UTI were collected from medical records department (MRD). The demographic data and prescription pattern of each case sheet were evaluated. The data obtained was subjected to descriptive statistical analysis using Microsoft excel.

Result: Total 108 patients were included in the study, out of which 44.4% were males and 55.6% were females. Most of the patients were in 40-60 years age group (40.7%). UTI confirmed by culture in 59.26% patients; in which E.coli was isolated in 35.9% patients followed by Klebsiella species (14.06%) and Pseudomonas aerugenosa (7.8%). The World Health Organization (WHO) indicators (utilization in defined daily doses (DDD); DDD/1000inhabitant/day) were used and the ATC/DDD method was implemented. The most commonly prescribed antimicrobial was ceftriaxone followed by cefixime and azithromycin.

Conclusion: The DDD/1000inhabitant/day of ceftriaxone was the highest (12.9). Third generation cephalosporins were used as first line drug in most cases. This group should be reserved for complicated UTIs.

Key words: DDD (defined daily dose), WHO indicators, ceftriaxone, generic names.

INRODUCTION

Drug utilization has been defined as the marketing, distribution, prescription and use of drugs on society with special emphasis on the resulting medical and social consequences.[1] Drug utilization studies are playing a major role in identifying any faults in the therapy and also find out solutions to rectify the same.

Rational drug prescribing is defined as "the use of the least number of drugs to obtain the best possible effect in the shortest period and at a reasonable cost."[2-4]Monitoring of prescription and drug utilization studies could identify the associated problems and provide feedback to the prescriber so as to create awareness about the irrational use of drugs.[5-7]It is necessary to define the prescribing pattern and to target the irrational prescribing habit for sending remedial message.[8]

Urinary tract infection (UTI) is defined as the presence of bacteria in urine along with symptoms of infection.[9]UTI is an extremely common condition

that occurs in both male and female of all the ages. The prevalence and incidence of UTI is higher in women than in men due to several clinical factors including anatomic differences, hormonal effects and behavioral pattern.[10]Etiology is influenced by factors such as age, diabetes, spinal cord injury, urinary catheterization, and other factors.[11]UTI is mostly caused by gram negative aerobic bacilli found in GI tract. These are *E. coli, Klebsiella, Enterobactor, Citrobacter andProteus*. Other common pathogens include *Staphylococcus epidermidis,Staphylococcus saprophyticus*and *Enterococcusspecies* which presumably result in UTI following colonization of the vagina or perianal skin.[12]

Drug utilization studies aids in commenting about unnecessary and irrational prescribing which increases burden of cost of therapy, also causes loss of working hours; either due to hospitalization or morbidity.[13]These are definitely not affordable for a developing country like India. In the recent years studies on drug utilization have become a potential tool to be used in the evaluation of health systems. The methodology used in these studies has mainly consisted in the comparison of consumption using defined daily doses (DDD) of the drugs consumed.

Drug utilization among outpatient is frequently monitored in many countries but the studies on inpatient are rare and incomplete. Studies of drug utilization in urinary tract infection are low. The objective of present study is to focus on the trends in the antimicrobial utilization in urinary tract infections. This information is not disease specific but reflects overall rates and illustrates trends in utilization of antimicrobials in the treatment of urinary tract infection.

MATERIALS AND METHODS

The study was conducted in the Department of Pharmacology, Krishna Institute Medical Sciences, Karad, Maharashtra.This is the retrospective record based study of patients admitted to Krishna Hospital and Research Centre, Karad, Maharashtra with diagnosis of UTI during the period of September 2012 to February 2013.The case sheets were collected from the medical records department (MRD) based on the ICD-10 disease coding.The demographic data and prescription pattern of each case sheet were evaluated in detail. The relevant investigations (microbiological and hematological) were noted down along with the urine culture report wherever available with the antimicrobial sensitivity testing. Comorbid conditions were noted down. Dose, frequency and duration of treatment with antimicrobial used to treat the urinary tract infection were recorded.

Anatomical therapeutic chemical (ATC) classification and defined daily dose (DDD) system was used for the quantification of drug utilization. Following formula of defined daily dose was used for calculation and results obtained were expressed in terms of defined daily dose per 1000 inhabitants per day (DDD/1000 inhabitants/day).[14] DDD/1000 inhabitants/day may provide a rough estimate of the proportion of the study population that may be treated daily with certain drugs. Condition of patient at the time of discharge was also noted. Descriptive statistics were used to describe the antimicrobial utilization pattern.

Formula: DDD/1000 inhabitants/day =

$$\frac{\text{Total drug used (mg) during the study period} \times 1000}{\text{DDD(mg)} \times \text{Duration of study} \times \text{Total sample size}}$$

Permission was obtained from the ethics committee of the institution for conducting the study. The purpose of the study was explained and confidentiality was ensured.

RESULTS

The study observed the drug utilization pattern to the patients treated to urinary tract infection in tertiary care teaching hospital, Karad. A total of 108 case records of the patients with different presenting symptoms were analysed.

All the case records had the complete documentation of information, including patient's demographic characteristics, diagnosis, culture and sensitivity wherever available, drug names, dose route and frequency of intake. Observations of the study are presented in the form of different tables.

Demographic characteristics showed UTI was more frequent in the age group of 40-60 years. UTI was equally frequent in both gender in <10 year age group; increased frequency in females from 10-60 years, but male had higher frequency after 60 years. (Table 1)

Table 1: The demographic data of patients

Age group (years)	Male (%)	Female (%)	Total (%)
<10	1 (50)	1 (50)	2 (1.9)
10-20	1 (25)	3 (75)	4 (3.7)
20-40	6 (31.6)	13 (68.4)	19 (17.6)
40-60	15 (34.1)	29 (65.9)	44 (40.7)
>60	25 (64.1)	14 (35.9)	39 (36.1)
TOTAL	48 (44.4)	60 (55.6)	108 (100)

Table 2: Isolated organisms in urine culture

Organisms	No. (%)
E Coli	23 (54.76)
P Aeruginosa	5 (11.90)
Proteus	3 (7.14)
Hemolytic Streptococci	2 (4.76)
Non Hemolytic Streptococci	2 (4.76)
Klebsiella Species	9 (21.42)
Coagulase +veStaphalococcus Aureus	5 (11.90)
Citrobacter Species	1 (2.38)
Candida Species	3 (7.14)
Acinobacter	1 (2.38)

Table 3: Antimicrobials resistant to E. coli

Resistant to	No of E.coli (%)
Ampicillin	20 (86.95)
Ceftriaxone	19 (82.60)
Ticarcillin	18 (78.26)
Carbanicillin	17 (73.91)
Norfloxacin	16 (69.56)
Nalidixic Acid	15 (65.21)
Bactrim	15 (65.21)
Cefotaxime	14 (60.86)
Gentamicin	14 (60.86)
Piperacillin	10 (43.48)
Ciprofloxacin	6 (26.08)

Table 4: Antimicrobials sensitive to E. coli

Sensitive to	No of E.coli (%)
Amikacin	21 (91.30)
Nitrofurantoin	13 (56.52)
Netilmicin	12 (52.17)
Gentamicin	9 (39.13)
Imipenem	5 (21.74)
Ceftriaxone	3 (13.04)

Table 5: Distribution of individual AMAs

Group	Drug	No. (%)
Flouroquinolones	Ciprofloxacin iv	24 (22.22)
	Ciprofloxacin oral	10 (9.25)
Penicillins	Amox.+ Clavul. acid iv	5 (4.62)
	Amox.+ Clavul. acid oral	3 (2.77)
	Piperacillin iv	4 (3.70)
β lactamase inhibi-	Sulbactam iv	5 (4.62)
tors	Tazobactam iv	6 (5.55)
Cephalosporins	Ceftriaxone iv	61 (56.48)
	Cefixime oral	20 (18.51)
	Cefpodoxime oral	12 (11.11)
Aminoglycosides	Amikacin iv	14 (12.96)
Macrolides	Azithromycin oral	19 (17.59)
Urinary antiseptics	Nitrofurantoin oral	12 (11.11)

*Amoxicillin + Clavulanic acid

Diabetes mellitus was most common comorbid condition followed by hypertension and renal or ureteric calculi. Urine culture was done in 59.26% (n=64) patients, out of which culture was positive in 65.63% (n=42) patients, sterile in 26.56% (n=17) patients and no significant growth in 7.81% (n=5) patients. In the remaining patients (n=44) the diagnosis was based on the clinical symptoms and microscopic examination of the urine which showed the presence of significant number of bacteria or pus cells. E. coli was the most common isolated organisms in urine culture. (Table 2)

Since E. coli (n=23) was the most common isolated organism, so the antimicrobial sensitivity pattern of E. coli has studied in detail. (Table 3 and 4) E. coli was resistant to ampicillin in 86.96% (n=20) patients and to ceftriaxone in 82.61% (n=19) patients and it was sensitive to amikacin in 91.3% (n=21) patients but to ceftriaxone only in 13.04% (n=3) patients.

Distribution of antimicrobial utilization was studied in detail. (Table 5) Cephalosporins were most commonly used antimicrobial followed by fluoroquinolones. Among the cephalosporins, third generation parenteral cephalosporins (ceftriaxone, cefotaxime, cefoperazone) were used most commonly and were switched over to the third generation oral cephalosporin (cefixime) in 20 patients after 4th or 5th day. Ciprofloxacin was the most commonly used fluoroquinolone which was shifted from parenteral to oral after 4 days in 10 patients. Among penicillins, amoxicillin + clavulanic acid combination was used in 9 patients followed by piperacillin + tazobactam

in 4 patients. Amikacin was the most commonly used aminoglycoside.

Drug consumption data were expressed as defined daily doses (DDD) per 1000 inhabitants per day. The highest value of 12.91 DDD /1000 inhabitants /day was accounted for ceftriaxone indicating that it was the popular drug of choice as a broad spectrum antimicrobial agent, followed by azithromycin with the value of 5.68 DDD /1000 inhabitants /day. (Table 6)

Table 6: ATC code, DDD, PDD and DDD/1000inhabitants/day of the drugs

Group	Drug	ATC code	DDD (mg)	PDD	DDDs / 1000 inhabitants / day
Sulfonamides	Sulfamethoxazole oral	J01EC01	2000	1200	0.314
Fluoroquinolones	Norfloxacin oral	J01MA06	800	850	0.742
	Ciprofloxacin iv	J01MA02	1000	455.91	1.852
	Ciprofloxacin oral		500	896.77	2.428
	Ofloxacin oral	J01MA01	400	400	0.044
	Levofloxacin oral	J01MA12	500	500	1.179
Penicillins	Cloxacillin iv	J01CF02	2000	500	0.055
	Ampicillin iv	J01CA01	2000	500	0.055
	Ampicillin oral		2000	2000	0.218
	Amoxicillin iv	J01CA04	1000	1714.3	2.096
	Amoxicillin oral		1000	1000	0.393
	Piperacillin iv	J01CA12	14000	13647	0.724
β lactamase inhibitors	Clavulanic acid iv	NA	NA	342.86	
	Clavulanic acid oral		NA	250	
	Sulbactam iv	J01CG01	1000	980.77	1.114
	Tazobactam iv	J01CG02	NA	1240	
Cephalosporins	Cefuroxime oral	J01DC02	500	1000	0.611
	Cefotaxime iv	J01DD01	4000	3000	0.491
	Ceftriaxone iv	J01DD04	2000	2052.1	12.91
	Ceftazidime iv	J01DD02	4000	2000	0.022
	Cefoperazone iv	J01DD12	4000	2000	0.197
	Cefixime oral	J01DD08	400	405.26	1.682
	Cefpodoxime oral	J01DD13	400	333.33	0.874
	Cefepime iv	J01DE01	2000	2000	0.961
Carbapenems	Meropenem iv	J01DH02	2000	3000	0.393
	Faropenem oral	J01DI03	NA	400	
Tetracyclines	Doxycycline oral	J01AA02	100	220	0.48
Aminoglycosides	Gentamicin iv	J01GB03	240	103.08	0.244
	Amikacin iv	J01GB06	1000	587.93	1.489
	Netilmicin iv	J01GB07	350	450	0.056
Macrolides	Azithromycin oral	J01FA10	300	500	5.678
Urinary antiseptics	Nitrofurantoin oral	J01XE01	200	252.38	2.315

Table 7: Comparison of PDD and DDD

PDD > DDD	PDD < DDD	PDD = DDD
Norfloxacin oral	Ciprofloxacin iv	Ofloxacin oral
Ciprofloxacin oral	Cloxacillin iv	Levofloxacin oral
Amoxicillin iv	Ampicillin iv	Ampicillin oral
Cefuroxime oral	Piperacillin iv	Amoxicillin oral
Ceftriaxone iv	Sulbactam iv	Cefepime iv
Cefixime oral	Cefotaxime iv	
Meropenem iv	Ceftazidime iv	
Doxycycline oral	Cefoperazone iv	
Netilmicin iv	Cefpodoxime oral	
Azithromycin oral	Gentamicin iv	
Nitrofurantoin oral	Amikacin iv	

Comparison of DDD and PDD (prescribed daily dose) was shown in Table 7. PDD>DDD was for the antimicrobials such as norfloxacin, ciprofloxacin, amoxicillin; PDD<DDD was for the antimicrobials such as ampicillin, amikacin, gentamicin and PDD=DDD was for the ofloxacin, levofloxacin and cefepime.

DISCUSSION AND CONCLUSION

In general practice, the therapeutic approach for urinary tract infection is primarily empirical and the

main aim of the physicians is to treat as specifically as possible. The present study indicates the general trends of use of antimicrobials in urinary tract infection.

Drug utilization studies have the potential to make objective evaluation and analysis of health professionals work and provide them with feedback to stimulate thinking about their practice and looking for ways to improve their own performance. These studies should become a method of increasing job satisfaction and means of education for health professionals, rather than being perceived as threat or another bureaucratic burden.[15] Antibiotic resistance is an emerging problem and has become a major threat to the medical field. Excessive and in appropriate use of antibiotic has been a major contributor to this ever growing problem.[16]

In contrast to the results of the study Qureshi AM.,[17] this study reveals frequency of UTI is equal in children of less than 10 years age in both male and female. Present study also reveals that the increased frequency of UTI in females in the age group of 40-60 years of age and increased frequency in males after the age of 60 years. This may be due the increased comorbid condition of diabetes mellitus in male patients after 60 years of age. These results coincide with Mahesh E. et al.[18] and Pargavi B. et al.[19]

As the results of the study Pargavi B. et al.,[19] present study also shows E. coli was the most commonly isolated organism in urine culture. Cephalosporins were the most common antimicrobial group used in this study which is similar to the study done by Bay AG. et al.[20]wherein the study by J. Mohan et al.[21] reveals amikacin is the most commonly used antimicrobial.

The PDDcan vary according to both the illness treated and national therapy traditions. For anti-infective, for instance, PDDs vary according to the severity of the infection. The DDDs for most anti-infective are based on treatment of moderately severe infections. In hospital care, much higher doses are frequently used and this must be considered when using the DDD as a unit of measurement.[22]

To conclude, third generation cephalosporins were used most commonly as first line drug, this group should be reserved for complicated UTIs.Periodic review of antimicrobial sensitivity should be done, to change the empirical treatment of urinary tract infections.These results highlight the need to educate the health care system to improve the adherence towards the standard guidelines for treatment of UTI.

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