

Prescription pattern of antibiotic usage for urinary tract infection treated in a rural tertiary care hospital.

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ABSTRACT

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Urinary tract infections are the second most common infectious disease in the community medical practice. The objective was to study the prescription pattern of antibiotics used in the treatment of UTI. A prospective cross sectional study was conducted on patients diagnosed with UTI. The study was carried out in the General medicine, OBG, Surgery and Urology departments of both in-patients and out-patients, for a period of 9 months (June 2010 to Feb 2011). Urinary Tract Infection patients who were in the age group of 18-80 years were included after obtaining their informed consent. A suitable data collection form was prepared and used to collect the required data. Among 136 patients, 41 were in-patients and 95 were out-patients. Most of the in-patients were prescribed with Ceftriaxone 28(68.3%), Cefotaxim 5(12.2%), and Ciprofloxacin 3(7.3%) respectively. In out-patients, Ciprofloxacin 27(28.4%), Norfloxacin 21(22.1%) and Nitrofurantoin 18(18.9%) were prescribed respectively. The study found that gram negative organisms like *E. coli* was the most predominant organism. It was also found that Cephalosporins were most commonly used and Quinolones were the second most commonly used drugs for the treatment of UTI. The third category drug used in UTI female patients was nitrofurantoin which is relatively inexpensive and safe for both pregnant and non-pregnant women.

Keywords: Urinary tract infection, Antibiotics, Prescription.

INTRODUCTION

Urinary tract infection (UTI) is also defined as the presence of micro-organisms in the urine that cannot be accounted by contamination. The organisms have the potential to invade the tissues of the urinary tract and adjacent structures.¹

Urinary tract infection 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 patterns.² A foreign body in the urinary system may act as a nidus for infection and may be associated with recurrent infections which may be due to calculi and indwelling catheters. Post – menopausal women are at higher risk for UTI than younger women, because they lack estrogen, which is essential to maintain the normal acidity of vaginal fluid. *E. coli* accounts for approx 85% of community acquired urinary tract infections and 50% of hospital acquired UTIs. Non-bacterial infections are less

common and tend to occur more often in immunosuppressed individuals or those with Diabetes Mellitus.²

Urinary tract infection in pregnancy may result in low birth weight infants, premature delivery and occasionally stillbirth. It is well documented that effective treatment of UTI's significantly reduces the incidence of pyelonephritis, premature deliveries and low birth weight infants.

The practice of prescribing antibacterial drugs for pregnant Urinary Tract Infection patients varies in different countries. Apart from economic factors, the problem of selecting an antibacterial agent for treatment of UTI in pregnancy is the possible confusion between a well established and well tolerated drug and empirically known to be harmless to the fetus, and also a drug to which there is a low level of bacterial resistance.

The general drugs prescribed for uncomplicated urinary tract infections are trimethoprim, nitrofurantoin and norfloxacin, ciprofloxacin and cotrimoxazole for Nitrofurantion is the commonly used drug to treat UTIs in pregnancy.³

Prescribing drugs is an important skill which needs to be continuously assessed and refined accordingly. Commonly, the prescription behavior is influenced by many factors like

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unethical drug promotion, lack of knowledge, direct consumer advertising and non-availability of drugs. So there is a chance of prescribing irrational drugs.

The assessment of the prescription will help to know the attitude of the physicians towards their prescribing, their therapeutic knowledge upgrading need/requirement and to ensure rationality in the prescription. The rationality of the prescriptions will help the physician in selecting the most appropriate cost effective treatment.⁴

No similar study has been conducted in this set-up previously. The antibiotic usage study in UTI, data will help in establishing a proper antibiotic utilisation guideline and promotes the rational prescribing of medicines. Hence, the present study was taken up to study the prescription pattern of antibiotics usage for urinary tract infection patients at rural tertiary care hospital.

MATERIAL AND METHOD

This was a prospective cross sectional study conducted in the General medicine, OBG, Surgery and Urology departments of Adichunchanagiri Hospital and Research Centre; B.G. Nagara, for a period of 9 months (June 2010-Feb 2011).

Ethical committee clearance was obtained on 22/6/2010 (Ref: AIMS/EC/601/2010-11) from Adichunchanagiri Hospital and Research Centre.

Study criteria:

1. Inclusion Criteria

Urinary tract infection patients (i.e. both recently diagnosed and recurrent UTI patients) treated with antibiotics in the age group of 18 to 80 years.

2. Exclusion Criteria:

Patients visiting departments other than OBG, General Medicine, Surgery and Urology and below 18 years of age. Because most of the UTI cases were observed only in the said departments and there is a good cooperation/encouragement of health care professionals. Very few/rarely, the UTI cases were observed in the pediatric population.

Sources of data:

- Patient case sheet, medication chart and lab reports.
- Patient interview.

Study procedure:

Prescriptions of out-patients and the treatment charts of in-patients were reviewed for the treatment of the UTI in

different departments. Patient consent was obtained before collecting the required data.

Determination of Prescription Pattern:

Patients diagnosed with UTI were interviewed to collect the socio-demographics and therapeutic data such as drugs prescribed, doses, route of administration, duration and other laboratory data were obtained by reviewing treatment charts and prescriptions. The follow-up of the patients was done everyday for in-patients and weekly once for out-patients. The changes in the prescribing drugs or their doses or duration were also documented. The drug-drug interactions were identified by using the MICROMEDEX software and also using the tertiary sources available in the library. Drug interactions were classified based on the severity and onset. Safety of antibiotics in pregnancy was assessed by using the tertiary sources such as Drugs in Pregnancy and Lactation and Lexi Company's Drug Information Hand Book. The category of the antibiotic and possible side effects due to the drug to both mother and the fetus were checked from the available sources.

Statistical methods: Descriptive statistical analysis has been carried out in the present study.

RESULTS

A total of 600 prescriptions were screened for UTI patients, in the outpatient department of OBG, General Medicine, Surgery and Urology departments, in which 95 UTI prescriptions were found and showed an antibiotic for its treatment. For in-patients nearly 226 case records have been reviewed, out of which 41 UTI case records have been identified and which was prescribed with antibiotics for treatment. Among in-patients, male were 25 and female were 16. In out-patients, male were 14 and female were 81.

Out of 136 patients, female patients were 97(71.3%) and male were 39(28.7%) respectively. Table.1 shows the incidence of UTI in male was more in patients with age group of 61-70 years 12 (30.8%) and least in age group of 51-60 (10.3%) & 71-80 (10.3%). There was no incidence of UTI in the age group of 18- 20 year in male patients. Out of 97 female patients, majority of the patients 31(31.9%) belongs to the age group of 21-30 years and least observed in the age group of 71-80 years i.e. 1(1.0%). The mean age distribution of the study population is 41.65 ± 16.87 .

The incidence of UTI cases admitted/referred to the OBG department were about 54.4% and 4.4% of cases to surgery department as shown in Table 2.

In our study, most of the in-patients were prescribed with empirical therapy with Ceftriaxone 28(68.3%) and drugs like Norfloxacin, Amikacin and Cefixime were prescribed to one patient each respectively. Drugs like Nitrofurantoin and Cephalexin were not prescribed to the in-patients, Ciprofloxacin is the most common drug prescribed among out-patients 27(28.4%). Female patients were more symptomatic (63.9%) compared to male(46.2%) with a P value =0.057+ . This was observed due to their hormonal changes and also due to their structural and anatomical difference. Culture sensitivity positive report was statistically similar in male 3(2.2%) and in female i.e. 9(9.3%) (P value=0.768).

Positive culture sensitivity reports of female UTI patients 6(6.2%) showed E.coli as a highest incidence of occurrence, where as other organisms like Citrobacter, Streptococcus and Proteus were found in 3 female patients respectively. Among 2 male positive culture sensitivity reports one presented with Citrobacter and the other with E.coli. In the remaining 124(91.2%) patients, culture sensitivity test was not performed, which shows that treatment was given empirically. Incidence of UTI recurrence was significantly more associated with male patients 33.3% compared to female 14.4% (P Value=0.012*). Incidence of recurrence is strongly significant in in-patients ($p=0.007^{**}$) as shown in the Table 3. One of the physical parameter observance/incidence like, urine appearance showed more turbidity in male 20(51.3%) than female 26(26.8%).

From among the study population of 136 patients, 5 drug-drug interactions were found, out of which 3 were moderately severe and the onset was rapid. Two interactions were found with major severity but the onset was unspecified, which is shown in Table 4 and 5. The overall rate of incidence of drug interaction was found to be 3.674%.

In pregnancy, the most commonly prescribed drug in first trimester was Nitrofurantoin (7) and the least was Trimethoprim(1). During the second trimester, Nitrofurantoin was prescribed in 3 patients and Ampicillin in 1 patient. During the third trimester, Cefixime and Cephalexin were prescribed in 4 patients respectively as represented in Table 6.

Ceftriaxone was most widely preferred drug to treat 28(68.3%) in-patients. Only 1(2.4%) patient was administered with Amikacin through IV route. Drugs such as Cefixime (1), Cefotaxime (2) and Amoxicillin (2) were also given to in-patients. The mean duration of treatment for in-patients was 6.32 days. Maximum number out-patients 26

were prescribed with Ciprofloxacin, followed by Norfloxacin in 21 patients, Nitrofurantoin to 18 patients. Mean duration of treatment for out-patients was 6.80 days as shown in Table 7.

DISCUSSION

The study of prescribing pattern is a component of medical audit, which seeks monitoring, evaluation in the prescribing practices of prescribers to achieve rational and cost effective medical care. It is necessary to define prescribing pattern and to identify irrational prescribing habits to drive a remedial message to the prescribers.

Our study showed that, majority of UTI patients were female mainly due to the structural and anatomical differences like shorter urethra. The same observations were made by several resources like Tomas.L, Greibling studies, and text books of pharmacotherapeutics by Herfindal and Roger walker.^{2, 5, 6} The present study was conducted in the age group of 18 – 80 years. The mean age of male was found to be 52.10 ± 17.41 and in female was 37.44 ± 14.77 . The mean age of the total study population was 41.65 ± 16.87 . Majority of female patients 31(31.9%) showed the incidence of UTI at the age group of 21-30 years, which is the child bearing age as well as sexually active period. During the post-menopausal period, most of the women shows the chances of UTI and its symptoms, this is also observed in our study. Twenty five (25.8%) female patients in the age group of 41-50 years were presented with UTI, similar results were observed and reported by William Bakey.⁷

The present study included 136 as the total number of patients, out of which 41 were inpatients and 95 were outpatients. Maximum of the females visited OBG department 74(76.2%) and minimum to surgery department 1(1.0%). Males 24(61.5%) mostly visited to the department of general medicine and least number of males 5(12.8%) visited to the department of surgery. Ten males (25.6%) visited urology department whereas females were only 5 (5.1%). Female UTI patients who visited the OBG department were more because of female patients generally prefer to check/diagnose with the same gender, for exchange of information freely and more availability of female doctors. Some female patients who visited this department for UTI complications, their final diagnosis report confirmed that either they were pregnant or diabetic along with UTI.

Among 39 male patients 21 (53.8%) were asymptomatic and 18(46.2%) were symptomatic. Among 97 female patients, 62(63.9%) were symptomatic and the remaining 35(36.1%) were asymptomatic with a suggestive significant value.

Table 1: Age wise distribution of the patients

Age in years	Male		Female		Total	
	N	%	N	%	N	%
18-20	0	0.0	10	10.3	10	7.4
21-30	6	15.4	31	31.9	37	27.2
31-40	5	12.8	13	13.4	18	13.2
41-50	8	20.5	25	25.8	33	24.3
51-60	4	10.3	9	9.3	13	9.5
61-70	12	30.8	8	8.2	20	14.7
71-80	4	10.3	1	1.0	5	3.7
Total	39	100.0	97	100.0	136	100.0
Mean $\pm$ SD	52.10 $\pm$ 17.41		37.44 $\pm$ 14.77		41.65 $\pm$ 16.87	

Table 2: Distribution of patients based on the department wise

Department	Male		Female		Total	
	N	%	N	%	N	%
Medicine	24	61.5	17	17.5	41	30.1
OBG	0	0.0	74	76.2	74	54.4
Surgery	5	12.8	1	1.0	6	4.4
Urology	10	25.6	5	5.1	15	11.0
Total	39	100.0	97	100.0	136	100.0

OBG: Obstetrics and Gynecology, N: Total number of patients.

Table 3: Incidence of Recurrence

Incidence of recurrence	IP		OP		Total	
	N	%	N	%	N	%
Observed	15	36.6	15	15.8	30	22.1
Not Observed	26	63.4	80	84.2	106	77.9
Total	41	100.0	95	100.0	136	100.0
Inference	Incidence of recurrence is significantly associated with Inpatients with a P Value=0.007**					

IP-Inpatients; OP- Outpatients; N- Total number of Patients.

Table 4: Evaluation of Drug - Drug interactions based on severity

Index drug	Interacting Drug	Interacting effect	Severity		
			Major	Moderate	Minor
Ciprofloxacin	Diclofenac	Increased ciprofloxacin plasma concentrations	-	Yes	-
Ciprofloxacin	Diclofenac	Increased ciprofloxacin plasma concentrations	-	Yes	-
Ciprofloxacin	Glimipride	Changes in blood glucose and increased risk of hypoglycemia or hyperglycemia	Yes	-	-
Norfloxacin	Iron	Decreased norfloxacin effectiveness	-	Yes	-
Levofloxacin	Insulin	Changes in blood glucose and increased risk of hypoglycemia or hyperglycemia	Yes	-	-

Table 5: Evaluation of Drug - Drug interactions based on onset

Index drug	Interacting drug	Onset		
		Rapid	Delayed	Unspecified
Ciprofloxacin	Diclofenac	-	-	Yes
Ciprofloxacin	Diclofenac	-	-	Yes
Ciprofloxacin	Glimipride	Yes	-	-
Norfloxacin	Iron	Yes	-	-
Levofloxacin	Insulin	Yes	-	-

Table 6: Assessment of antibiotic safety in pregnancy

Drugs	Pregnant			Category
	1 st trimester N	2 nd trimester N	3 rd trimester N	
Nitrofurantoin	7	3	0	B
Cefixime	0	2	4	B
Cephalexin	1	0	4	B
Ampicillin	0	1	0	B
Trimethoprim	1	0	0	B
Total	9	6	8	

N – Number of patients

Table 7: Comparison of antibiotic use between inpatients and outpatients

Prescribing pattern of antibiotics	IP					OP				
	N	%	Duration	Oral	IV	N	%	Duration	Oral	IV
Ceftriaxone	28	68.3	5.39	0	28	2	2.1	7.00	2	0
Ciprofloxacin	3	7.3	6.50	0	3	27	28.4	6.35	26	0
Norfloxacin	1	2.4	8.00	0	1	21	22.1	7.29	21	0
Nitrofurantoin	0	0.0	-	0	0	18	18.9	6.44	18	0
Cefixime	1	2.4	3.00	1	0	9	9.5	4.56	9	0
Cefotaxim	5	12.2	10.40	2	3	2	2.1	18.50	2	0
Cephalexin	0	0.0	-	0	0	7	7.4	5.29	7	0
Amoxicillin	2	4.8	7.00	2	0	5	5.3	7.17	6	0
Amikacin	1	2.4	12.00	0	1	3	3.2	11.67	3	0
Others	0	0.0	-	0	0	1	1.1	5.00	1	0
Total	41	100.0	6.32	5	36	95	100.0	6.80	95	0

IP: Inpatient, OP: Outpatient, N: Total number of patients, IV: Intravenous.

Symptomatic UTIs can occur essentially in all age groups of the population but are most prevalent in females. The same observations were identified in the epidemiology of urinary tract infection.⁵

Among 136 patients, culture sensitivity test was performed only for 12(8.8%) out of which 3(2.2%) were male and 9(9.3%) were female. Culture sensitivity tests were not performed in 124(91.2%) patients because of non-affordability or financial/socio-economic issues of the rural patients. The results of culture sensitivity in 12 patients showed presence of *Citrobacter* species 2(1.5%) of male and

1(1.0%) in female. The highest incidence of micro organism was *E. Coli* found in 6(6.2) females and 1(0.7%) male. In our study we found that 2 elderly Benign prostrate hyperplasia male's urine sample culture sensitivity tests showed *Citrobacter* species for symptoms of UTI. Similar observations were found in other case reports.¹¹ *Proteus* and *Streptococcus* organisms were found in 1(1.0%) female patient each. The study also found that *E. coli* was the most predominant organism. This finding is in concordance with the other study^{9,12,13} The incidence of recurrence is associated more in male 13(33.3%) than female 14(14.4%) because of

their associated disease conditions like Hypertension, Chronic Kidney disease and Diabetes.

The prescribing pattern of antibiotics usage study in in-patients and out-patients showed 10 types of antibiotics prescribed. Ceftriaxone was prescribed to in-patients 28(68.3%), whereas it was prescribed for 2(2.1%) out-patients. Ciprofloxacin prescribed in in-patients was 3(7.3%) and out-patients was 27 (28.4%). Norfloxacin was prescribed to 1(2.4%) in in-patients and 21(22.1%) out-patients. Nitrofurantoin was prescribed to 18(18.9%) out-patients. Cefixime was prescribed in 1 in-patient (2.4%) and 9(9.5%) out-patients. Cefotaxim was prescribed to 5(12.2%) of in-patients and 2(2.1%) of out-patients. Seven out-patients were prescribed with Cephalexin at the rate of 7.4%. Among the total of seven Amoxicillin prescriptions 2(4.8%) belongs to in-patients and the rest of 5(5.3%) were given to out-patients. Four Amikacin prescriptions were present, 1(2.4%) for in-patients and 3(3.2%) for out-patients. Only one out-patient was prescribed with drug of other category at the rate of 1.1%.

Cephalosporin's and Fluoroquinolones was the most commonly used antibiotics in the hospital practice for the treatment of UTI.^{8,9} Fluoroquinolones remains the choice among the orally administered antibiotics, followed by second and third generation Cephalosporin's. The prescribing pattern of antibiotics for the treatment of UTI in our hospital, showed that Cephalosporin's 54 (55.6%) and Quinolones 52(47.1%) was most commonly prescribed antibiotics. Similar findings were observed in the studies conducted by Mathi E et al and Joe et al and Kallen et al.^{8,9,10}

The commonly occurring drug interactions were found with fluoroquinolone antibiotics so monitoring of such prescription by the pharmacist will helped in avoiding of further problems by using suitable strategies.

Our study also found the antibiotics safety in pregnancy UTI. This showed that nitrofurantoin is safe and efficacious in I and II trimester. This drug is not recommended in the third trimester due to haemolytic effects. The safe use of antibiotics was observed with cephalosporins like cefixime and cephelexine in the third trimester. Similar study supported by Cimoli and Kay sam.^{14,15}

The inappropriate selection and use of antibiotic not only causes resistance but also causes more harm thus leading to recurrence of the UTI. Concerns about increased resistance have contributed to greater use of fluoroquinolones, but widespread empiric use of this class of medications might promote resistance to fluoroquinolones. Hence,

fluoroquinolones should not be considered as first-line therapy. While guidelines for treatment of UTIs have been developed, their usefulness is compromised by their conflicting recommendations.¹⁶ This is also seen in 4 year descriptive study by Laura G Aurelio S.^{16,17}

The main limitation of this study was, short duration and less number of pregnant UTI patients enrolment.

Our study showed a few potential directions for future research are establishing of antibiotic guidelines for UTI, prescribing pattern study in Pregnant UTI in large samples and antibiotic resistance studies.

CONCLUSION

Complications from inadequately treated UTIs contribute to increased patient morbidity, increased health care costs, and increased drug resistance. The study found that E. coli was the most predominant organism. It was also found that Cephalosporin's were most commonly used and Quinolones were the second most commonly used drugs, for the treatment of UTI. Nitrofurantoin, a relatively inexpensive and safe drug for the treatment of UTI was used in both pregnant and non pregnant patients. Widespread empirical use of Fluoroquinolones also might promote microbial resistance to Fluoroquinolone group of drugs. Hence, Fluoroquinolones should not be considered as first-line therapy. Our findings indicate an urgent need for the establishment of proper guidelines, dissemination of information to practitioners and supervision of antibiotic usage in low income countries like India.

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