



Prescribing pattern of fluoroquinolone antibiotics in medicine units of rural tertiary care teaching hospital in South India

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ABSTRACT

Background: Fluoroquinolones (FQs) are among the most commonly prescribed antimicrobials and are used inappropriately which may increase the risk of bacterial drug resistance.

Objective: To know the utilization pattern of Fluoroquinolones and give a review of the prescribing practice of physicians in rural hospital.

Methodology: A hospital based prospective and observational study was carried out in medicine units of tertiary care teaching hospital. The prescription was screened for utilization of FQs.

Results: Among 108 patients, 60 were males and 48 females. Total of 92.59% patients received Fluoroquinolones for empirical treatment. Ciprofloxacin was the most commonly used FQs. An average of 1.06 Fluoroquinolones per prescription was prescribed. Oral route was more preferred than the parenteral route for administration of FQs. Mean \pm SD number of drugs prescribed was 10.10 ± 3.16 and duration of hospitalization was 6.84 ± 3.77 days. Two cases of E. coli were resistance to Ofloxacin and Ciprofloxacin. Total of 72 possible Drug- Drug Interactions (DDIs) were identified in 54 patients. Out of which, 33 (45.83%) were accepted and necessary action was taken to minimize the risk of interaction.

Conclusion: The specific use of Fluoroquinolones based on culture test is necessary. The application of stewardship strategies increases physician awareness of guidelines improves appropriate antimicrobial use and reduces unnecessary antimicrobial prescribing. Prescription review by clinical pharmacists with feedback to the prescriber is needed to improve appropriate use of FQs, on time management of possible risk from drug interaction and avoidance of drug resistance.

Key words: Antibiotics, Fluoroquinolones (FQs), drug utilisation, antimicrobial resistance.

INTRODUCTION

Antibiotics deserve their place as one of the most powerful pillars of modern medical care and widely used medicines to treat both life threatening and trivial infections. In India, the prevalence of antibiotics use varies from 24-67% [1]. Although they have been dubbed “miracle drugs”, antibiotics are not always effective due to development of resistance. Thus, appropriate drug use utilization studies are important tools to evaluate whether antibiotics are properly utilized in terms of efficacy, safety, convenience and economic aspects at all level in the chain of drug use [2].

Fluoroquinolones account for about 11% of antimicrobial prescriptions in human medicine worldwide and represent the drug of choice for the

treatment of a wide range of human infectious diseases including UTI, respiratory tract infections, skin and soft tissue infections, bone and joint infections and infections in the ear and eyes. Following the Fluoroquinolones introduction, resistant strains of bacteria has started to emerge. In one study conducted in Europe suggested that there was decrease in susceptibility to Ciprofloxacin with *Klebsiella pneumonia* (7.2%) and *Klebsiella oxytoca* (3.4%) but Fluoroquinolones are on the WHO list of drugs that should be reserved for human use [3,4,5]. So study of prescribing pattern in a particular setting give an idea about the prescribing practices and characterizes the early signals of irrational drug use [6]. Therefore this prospective study is designed to identify the utilization of Fluoroquinolones and give a review of the prescribing practice of physicians in rural

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hospital which can be modified if necessary and facilitate better health care delivery and also helps to promote the rationality and minimising the errors in the drug therapy.

MATERIALS AND METHODS

This study was carried out in the medicine units of a 1050 bedded tertiary care teaching hospital. The study was conducted for a period of seven months from July 2014-february 2015. Permission was obtained from Institutional Ethics Committee before starting the study. The data were collected from patients of either sex above 18 years of age, who got admitted to the medicine units of the hospital and prescribed with Fluoroquinolones. A suitable data collection form was designed to collect and document the data. Data collection form includes demographic details of patient; drug therapy details (name of drug, dosage form, frequency, route of administration, duration of treatment) and length of stay. Data were collected from the patient's file on a daily basis. The incidence of Fluoroquinolones use was studied based on gender and age of patients. The total prescriptions were analysed for number of drugs per prescription and then the prescriptions were screened/evaluated for the common category of drug prescribed on the basis of essential medicine list 2013 for the disease condition, number of Fluoroquinolones antibiotics per prescription, type of therapy (Empirical or Specific), gender, dose, and route of administration, frequency of administration, culture and sensitivity (C&S) results, and duration of antibiotic therapy, also any major/potential drug interaction and ADRs if any using standard textbooks/ tertiary sources and software available in the department. The identified

drug related problems was discussed with the physicians for further management. The data were subjected to descriptive statistical analysis using Microsoft Excel. Microsoft word and Excel have been used to generate bar graph, pie charts and tables.

RESULTS

Total of 108 patients enrolled in study, males were 60 (55.56%) and females were 48 (44.44%). The majority of the patients (48.15%) were in the age group of 60-80 years followed by (30.56%) the age group of 40-60 (Table 1).

Total of 1091 drugs were prescribed to 108 patients with a mean \pm SD of drugs prescribed 10.10 \pm 3.1616 in which maximum number of patient i.e. 64 (59.26%) were prescribed with 6 to 10 numbers of drugs followed by 31 (28.70%) patients with 11 to 15 numbers of drugs (Table 2).

Among study population, 71 (65.75%) were having at least one co-morbidity condition whereas 37 (34.25%) were not having any co-morbidity condition. Out of 71 patients, 44 (61.97%) were having only one co-morbidity condition along with infectious disease followed by 18 (25.35%) were having two co-morbidity and 9 (12.68%) were having three or more than three co-morbidity condition (Table 3).

Maximum number of patients admitted in medicine units who were prescribed with Fluoroquinolones have infection in respiratory tract 48 (44.44%) followed by gastrointestinal tract 23 (21.29%) and urinary tract 14 (12.96%) (Table 4).

Table 1: Age distribution of patients

Age in years	Number of patients	Percentage (%)
<20	2	1.85
20-40	13	12.03
40-60	33	30.56
60-80	52	48.15
>80	8	7.41

Table 2: Number of drugs prescribed during hospital stay

Number of drugs in the prescription	Number of patients received	Percentage (%)
1-5	6	5.56
6-10	64	59.26
11-15	31	28.70
>15	7	6.48

Table 3: Distribution of co-morbidity condition

No. of co-morbidity condition	No. of patients	Percentage (%) (n=71)
1	44	61.97
2	18	25.35
≥3	9	12.68

Table 4: site of infection for Fluoroquinolones use

Site of infection	No. of patients	Percentage (%) (n= 108)
Eye	3	2.78
Eye / Respiratory tract (RT)	1	0.93
Respiratory tract (RT)	48	44.44
Gastrointestinal tract (GIT)	23	21.29
Urinary tract (UT)	14	12.96
Gastrointestinal tract / Respiratory tract	3	2.78
Gastrointestinal tract / Urinary tract	1	0.93
Respiratory tract / Urinary tract	7	6.48
Liver	5	4.63
Head	1	0.93
Foot	2	1.85

Out of 1091 drugs prescribed, the mostly prescribed therapeutic class of drugs during hospital stay were anti-infectives 271(24.84%), followed by respiratory system drugs 222 (20.35%) and alimentary tract drugs 157 (14.39%) (Table 5). Number of patients admitted for a period of 1 to 5 days was 56 (51.85%) followed by 39 (36.11%) patients for 6 to 10 day and 10 (9.26%) patients for 11 to 15 days. Mean \pm SD duration of hospital stay was 6.84 ± 3.77 days (Table 6). During the study period 60 (55.56%) patients received Fluoroquinolones for 5 days followed by 20 (18.51%) patients for 3 days (Table 7).

During the study period total of 115 Fluoroquinolones were prescribed to the study population with an average of 1.06 of Fluoroquinolones per prescription where only one Fluoroquinolone was prescribed in 101 (95.37%) patients and 7 (6.48%) patients were prescribed with two Fluoroquinolones during hospital stay. Among Fluoroquinolones, Ciprofloxacin 50 (43.48%) was most commonly prescribed followed by Levofloxacin 48 (41.74%). Ciprofloxacin was most commonly prescribed parenterally and Levofloxacin was prescribed orally. Moxifloxacin was only prescribed as eye drops (Table 8).

All Ciprofloxacin preparation was prescribed twice a day (BD) whereas Levofloxacin 45 (39.13%) was prescribed once a day (OD) and 3 (2.61%) twice a day (BD) followed by Norfloxacin 9 (7.83%) for BD, Ofloxacin 1 (0.87%) for OD and 3 (2.61%) for BD. Fluoroquinolones were mainly used as OD in respiratory diseases and as BD in gastrointestinal diseases followed by respiratory diseases. In the present study maximum number of patients 100 (92.59%) received empirical therapy whereas only 8 (7.41%) patients received specific therapy.

The most commonly prescribed anti-infectives along with Fluoroquinolones was ceftriaxone 36 (33.33%) followed by metronidazole 31(28.70%) (Table 9).

Total of 72 possible drug-drug interactions were identified in 54 patients. All the identified DDIs were reported to physicians and documented, out of which 33 (45.83%) were accepted and necessary action was taken to minimize the risk of interaction (Table 10). Majority of DDIs were pharmacodynamics and synergistic in nature. Most common drug interaction was observed between Ciprofloxacin and Ondansetron i.e. 15 (20.83%) followed by Ciprofloxacin and Insulin 10 (13.89%) (Table 11).

Table 5: Distribution of therapeutic classes of drugs prescribed during hospital stay

Therapeutic classes	Percentage (%) (n=1091)
Anti-infectives	24.84
Alimentary tract drugs	14.39
Hormones and other endocrine medicines	3.57
Cardiovascular drugs	7.24
Diuretics	2.57
Vitamins, minerals and proteins	4.58
Respiratory system drugs	20.35
Antiallergic and medicine used in anaphylaxis	1.28
Analgesics, antipyretics, NSAIDS, medicines for gout, rheumatoid disorders and migraine	8.07
Medicine affecting blood	0.73
Central nervous system drugs	1.83
Miscellaneous	10.54

Table 6: Duration of hospital stay

Number of days of hospital stay	Number of patients	Percentage (%)
1-5	56	51.85
6-10	39	36.11
11-15	10	9.26
>15	3	2.78

Table 7: Duration of Fluoroquinolones prescribed

Number of days Fluoroquinolones prescribed	Number of patient	Percentage (%)
1	1	0.93
2	7	6.48
3	20	18.51
4	9	8.33
5	60	55.56
6	1	0.93
7	8	7.40
9	1	0.93
15	1	0.93

Table 8: Individual Fluoroquinolones use

Fluoroquinolones (ATC Code)	Number			Percentage (%) (n=115)			Total (%)
	Parenteral	Oral	Eye drops	Parenteral	Oral	Eye drops	
Ciprofloxacin (J01MA02)	22	28	0	19.13	24.35	0	50 (43.48%)
Levofloxacin (J01MA12)	12	36	0	10.43	31.30	0	48 (41.74%)
Moxifloxacin (S01AE07)	0	0	4	0	0	3.48	4 (3.48%)
Norfloxacin (J01MA06)	0	9	0	0	7.83	0	9 (7.83%)
Ofloxacin (J01MA01)	0	4	0	0	3.48	0	4 (3.48%)
Total	34	77	4	29.56	66.96	3.48	115 (100%)

Table 9: Comparison of anti-infectives co-prescribed with Fluoroquinolones

Anti-infectives co-prescribed	Number of patients	Percentage(% in total patients)
Amoxicillin/clavulanate	4	3.70
Cefixime	3	2.78
Ceftriaxone/salbactam	4	3.70
Ceftriaxone	36	33.33
Azithromycin	5	4.63
Piperacillin/tazobactam	10	9.26
Doxycyclin	9	8.33
Amikacin	4	3.70
Gentamicin	1	0.93
Clindamycin	1	0.93
Linezolid	1	0.93
Meropenem	1	0.93
Metronidazole	31	28.70
Tinidazole	9	8.33
Nitrofurantoin	6	5.56

Table 10: Physician acceptance and action taken

Action taken	Number	Percentage (%) (n=33)
Dose altered	2	6.06
Frequency changed	7	21.21
Monitored therapy	23	69.70
Drug stopped	1	3.03

Table 11: DDIs identified during study period

Interacting drugs	No. of DDIs (Total =72)	Classification of DDI	
Levofloxacin + Ondansetron	7	Pharmacodynamic	Synergistic
Levofloxacin + Insulin	6	Pharmacodynamic	Synergistic/Antagonist
Ciprofloxacin + Ondansetron	15	Pharmacodynamic	Synergistic
Furosemide + Amikacin	1	Pharmacokinetic	Synergistic
Levofloxacin + Glibenclamide	2	Pharmacodynamic	Synergistic/Antagonist
Levofloxacin + Metformin	4	Pharmacodynamic	Synergistic/Antagonist
Ciprofloxacin + Insulin	10	Pharmacodynamic	Synergistic/Antagonist
Ciprofloxacin + Metformin	6	Pharmacodynamic	Synergistic/Antagonist
Levofloxacin + Mefloquine	2	Pharmacodynamic	Synergistic
Rifampicin + Phenytoin	1	Pharmacokinetic	Antagonist
Norfloxacin + Metformin	1	Pharmacodynamic	Synergistic/Antagonist
Norfloxacin + Glimipride	1	Pharmacodynamic	Synergistic/Antagonist
Atorvastatin + Carbamazepine	1	Pharmacokinetic	Antagonist
Atorvastatin + Fenofibrate	1	Pharmacodynamic	Synergistic
Ofloxacin + Insulin	1	Pharmacodynamic	Synergistic/Antagonist
Norfloxacin + Mefloquine	1	Pharmacodynamic	Synergistic
Norfloxacin + Ondansetron	1	Pharmacodynamic	Synergistic
Mefloquine + Ondansetron	2	Pharmacodynamic	Synergistic
Ciprofloxacin + Gliclazide	1	Pharmacodynamic	Synergistic/Antagonist
Ciprofloxacin + Theophylline	2	Pharmacokinetic	Synergistic
Levofloxacin + Glimipride	1	Pharmacodynamic	Synergistic/Antagonist
Levofloxacin + Theophylline	4	Pharmacokinetic	Synergistic
Alprazolam + Digoxine	1	Pharmacodynamic	Synergistic

DISCUSSION

The incidence of Fluoroquinolones prescription was higher in male compared to female. This finding is similar to other studies (Shankar Pk *et.al* and Joel JJ *et.al*) [7, 8]. Majority of the patients 52 (48.15%) were in the age group of 60-80 years followed by age group of 40-60 years, 33 (30.56%). Few study showed that the age group ranged from 40-80 years were more likely to be prescribed with Fluoroquinolones (Joel JJ *et.al* and Linder JA *et.al*) [8, 9].

About 65.75% of study population has been presented with at least one co-morbidity condition. The most common co-morbidity condition observed was hypertension and/or diabetes. These co-morbidity leads to the poly pharmacy and thus increases the chance of more drug related problems.

The study showed that more percentage of FQs was used for FDA-approved indication. Relating to the previous study conducted by Shankar et al [7] and Linder et.al [9] greater number of FQs were used for infection in respiratory tract, urinary tract and gastrointestinal tract.

Among the drugs prescribed to the study patients, anti-infective drugs (24.84%) were the most commonly prescribed class of drugs, followed by respiratory system drugs (20.35%) which were similar to the study conducted by Gordana P et al [10] where anti-infective for systemic use constitute the most utilized group. The use of drugs depends on the co-morbidity patterns and other factors and may not be comparable between different studies. It is obvious that the increased use of anti-infective agents and respiratory system drugs were due to the reason that most of the study population were presented with infectious disease of respiratory tract.

The mean \pm SD duration of hospital stay during study period was 6.84 ± 3.77 days ranging from 2 to 22 days which is similar to the study conducted in a teaching hospital, Nepal where mean \pm SD duration of hospital stay was 6.2 ± 5.4 days [7] whereas very less than that study conducted by the Joel et al (11.54 ± 7.57 days) [8]. In this study maximum numbers of patients were admitted for 1-5 days because the study site is situated in the rural area and maximum patients were of agricultural background and they demand for early discharge.

With an average of 1.06 fluoroquinolones per prescription, 25% patients were prescribed FQs as a single anti-infective agent. The effective use of

single anti-infectives in patients indicates the improved prescribing skill of the clinicians and also avoids the possible drug related problems. Out of 115 FQs prescribed 43.48% was Ciprofloxacin and 41.74% was Levofloxacin. In this study parenteral Ciprofloxacin (19.13%) was prescribed more than the parenteral Levofloxacin (10.43%) similar to the previous study [11] but in another study it was found that parenteral Levofloxacin was more than parenteral Ciprofloxacin [8].

In our study only 7.41% of patients received specific treatment and 92.59% patients were treated empirically wherein another study only 35% patients were treated empirically [8]. Patients were mostly prescribed with broad spectrum fluoroquinolones for empirical treatment. This study showed that treating of patients specifically after culture and sensitivity test is relatively low than empirical treatment. The most common clinical conditions that were treated empirically with FQs were lower respiratory tract infections {21 (20.59%)}, acute exacerbation of COPD {21 (20.59%)}, followed by acute gastroenteritis {20 (19.61)} and urinary tract infection {15 (14.71%)}. In another study FQs were empirically used in acute gastroenteritis (42.86%), lower respiratory tract infections (17.14%) [8].

Levofloxacin 75% was most commonly used Fluoroquinolone for specific treatment followed by Ciprofloxacin 25%. During the study period two cases of *E. coli* were found, in which one is resistant to Ofloxacin and another with Ciprofloxacin.

The most common anti-infectives co prescribed in medicine units was found to be ceftriaxone (33.33%) followed by metronidazole (13.86%) and piperacillin/tazobactam (9.26%). In a previous study conducted at same study site also shows that mostly prescribed anti-infectives was ceftriaxone (48.51%) followed by metronidazole (17.82%) and ciprofloxacin (13.86%) [12]. Another cross sectional study in two private sector hospitals conducted by Sharma *et al.* [13] also shows the similar result where ceftriaxone was mostly prescribed antibiotics followed by metronidazole. The prospective prescription audit, conducted by Gupta N *et al.* [14], showed different result than the present study where prescribing frequency for Penicillins and Cephalosporins was more followed by metronidazole.

During the study period total of 72 possible DDIs were identified among 54 (50%) patients. This finding was lower compared to other study conducted by Kumar *et.al.* Majority of DDIs were

pharmacodynamics and synergistic in nature. Out of 72 DDIs, 33 interactions (45.83%) were accepted by the physicians and took necessary action for further management after clinical pharmacist recommendation. The action taken for management of possible interaction was dose adjustment (60.6%), frequency changed (21.21%), monitored therapy (69.70%) and drug stopped (3.03%). It should be remembered that the clinical outcomes of most interactions is highly situational and depends on several factors including the sequence of administration, duration of therapy, dose of each drug and even the influence of other drugs[15].

CONCLUSION

The number of patients receiving specific treatment based on culture and sensitivity test was less than those reported in the previous studies. So there is need to increase in the specific treatment depending upon culture and sensitivity test to reduce the emergence of drug resistance. Involvement of clinical pharmacist in prescription analysis and

prescribing pattern studies can help provide feedback to the physicians on the current prescribing practices. This can further contribute in reducing the incidence of possible risk from drug interaction and promote rational prescribing of antibiotics.

The study opens door for larger studies to emphasize the role of clinical pharmacist in order to improve the irrational prescribing practice of antibiotics.

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