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A RETROSPECTIVE STUDY ON THE DRUG USAGE PATTERN OF CEPHALOSPORINS IN THE GENERAL MEDICINE DEPARTMENT

Karukakulam Sandra Dominic, Nandakumar U.P.* and Sharad Chand

[1]Department of Pharmacy Practice, Nitte Gulabi Shetty Memorial Institute of Pharmaceutical Sciences, Nitte (Deemed to be University), Mangaluru, Karnataka, India-575018

*Address correspondence Email: nandakumarvtkv@gmail.com

Abstract

To analyse the prescribing pattern of cephalosporins among patients admitted in the department of general medicine. A retrospective study was conducted for six months in the department of general medicine of Justice K.S. Hegde Charitable Hospital, Deralakatte, Mangaluru. The data of the patients who met the inclusion criteria was collected in a suitably designed data collection form. Relevant details of patients prescribed with cephalosporins such as their complete demographic profile, social habits, duration of hospital stay were obtained. Data including the name of cephalosporin agent administered, route of administration, co-prescribed drugs were also recorded. Out of 250 patients enrolled, males 132 (52.8%) were found to be predominant over the females 118 (47.2%). Majority of the patients 65 (26.8%) belonged to the age group of 18-29 years. 67 (26.8%) patients were diagnosed with lower respiratory tract infection followed by urinary tract infection and acute gastroenteritis, 32 (12.8%) each. Only third generation cephalosporin agents were prescribed among the subjects and ceftriaxone was found to be the highest prescribed among 159 (60.0%) patients. Majority of the subjects (86.4%) had intravenous route of administration of cephalosporins. 205 (82.0%) prescriptions used brand names of cephalosporin agents. Azithromycin (14.8%) and metronidazole (9.6%) were found to be the most commonly co-prescribed antibiotics. The most commonly prescribed cephalosporin antibiotic agent was found to be ceftriaxone, belonging to the third generation class. The study provides an insight to the healthcare professionals including clinical pharmacists on the need to work together for practicing rational use of antibiotics.

***Keywords*:** Antibiotics, cephalosporin, drug usage pattern, general medicine.

Introduction

Cephalosporins are the largest and the most diverse family of antibiotics available and possess an extended spectrum of activity. Cephalosporins possess a mechanism of action identical to penicillin; it inhibits transpeptidation process leading to the formation of imperfect cell wall, followed by a series of events finally leading to lysis of the bacteria (Gaundavar *et al*., 2016). Cephalosporins are divided into first, second, third, fourth and fifth generations depending upon their spectrum of activity (Sathyanarayan *et al*., 2016). The World Health Organization (WHO) defines drug utilization research as "the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences" (Al-Jabri *et al*., 2019 and Gouda *et al*., 2019). Drug utilization research studies conducted in the inpatient settings are effective tool that helps in evaluating the drug prescribing trends, cost effectiveness and efficiency of hospital formularies (D'souza, 2019). Conducting periodic studies of pattern of drug use in various hospital settings or patient populations is therefore essential to critically analyse the current hospital drug policies and to make recommendations to improve the drug usage pattern in the future, if needed (Chandran *et al*., 2020). Antibiotics are the most commonly used therapeutic agents, accounting for the majority of prescriptions, both in hospital setting as well as community setting. Surveys have shown that 22–65% of antibiotic prescriptions are either inappropriate or incorrect. Use of broad-spectrum antibiotics including cephalosporins have been linked to the emergence of antibiotic resistance and have warranted the need for Drug Utilization Evaluation (DUE). Hence, this study was conducted to analyse the prescribing pattern of cephalosporins among patients admitted in the department of general medicine.

Materials and Methods

A retrospective study was conducted in the department of general medicine of Justice K.S. Hegde Charitable Hospital, Mangaluru. Since it was a retrospective study of one year data (January 2016- December 2016), the minimum expected number satisfying the inclusion criteria was calculated as 250. Patients of either gender above 18 years of age, prescribed with cephalosporin antibiotics were included in the study. Ethical approval was obtained from the Institution Ethics Committee (IEC) Ref No: NGSMIPS/IEC/22/2018-19 before initiating the study. Data was collected after getting permission from the hospital and unit authorities. Details of the patients prescribed with cephalosporins such as their complete demographic profile, social habits, duration of hospital stay were obtained from the case records. Data including the name of cephalosporin agent administered, route of administration, co-prescribed drugs were also recorded.

Statistical analysis: Frequency and percentage were used to summarise the qualitative variables. Mean and standard deviation were used to analyse the quantitative variables. Data analysis was done by using SPSS (version 20.0)

Results

Distribution of subjects based on their gender

Among 250 subjects enrolled, majority 132 (52.8%) were males and 118 (47.2%) were females.

Distribution of subjects based on their age

Out of the total subjects enrolled, majority 65 (26.0%) were found to be belonging to the age group of 18-29 years**.** The mean age of the sample population was found to be 48.15 ± 18.94 SD years. Details are summarized in Table 1 and 2.

Distribution of subjects based on the length of hospital stay

The duration of hospital stay of enrolled subjects ranged from 1-28 days. The mean length of hospital stay of the subjects was found to be 7.14 ± 4.51standard deviation. Among 250 patients enrolled, majority 162 (64.8%) were found to have 1-7 days of hospital stay followed by 8-14 days, 69 (27.6%). Details are summarized in Table 3.

Distribution of subjects based on their social habits

Out of the total subjects enrolled, 40 (16.0%) were found to be present with at least one social habit. Among 40 subjects, majority were found to be alcoholic, 18 (45.0%), followed by subjects who had the habit of both alcohol consumption and cigarette smoking, 12 (30.0%). The details are summarized in Table 4.

Distribution of comorbid conditions reported among the subjects

Out of 250 subjects, 121 (48.4%) presented a total of 161 comorbid conditions. Among the various comorbidities reported, hypertension was found to be the highest, 73 (45.3%), followed by Diabetes Mellitus, 49 (30.4%). Details are summarised in Table 5.

Distribution of subjects based on diagnosis

Out of 250, majority of the subjects who received cephalosporin antibiotics were found to be diagnosed with lower respiratory tract infection (LRTI) 67 (26.8%), followed by urinary tract infection (UTI) and acute gastroenteritis, 32 (12.8%) each. Details are summarised in Table 6.

Distribution of subjects based on the number of drugs prescribed

Among 250 subjects, the minimum number of drugs prescribed per patient was found to be 3 and the maximum was 22. The mean number of drugs per prescription was found to be 8.71 ±3.68 SD and cephalosporin antibiotic per prescription was 1.06 ± 0.23.

Prescribing pattern of cephalosporin agents

Only third-generation cephalosporins were found to be prescribed among 250 study subjects, in which Ceftriaxone was found to be the highest prescribed agent, 159 (60.0%), followed by Ceftriaxone+ Tazobactam, 41 (15.5%). Detailed summary of the result is given in Table 7.

Distribution of subjects based on brand and generic prescription of cephalosporins

In brand versus generic analysis, 205 (82.0%) prescriptions out of 250 were prescribed by brand names and 45 (18%) prescriptions were given by generic names.

Distribution of patients based on route of administration of cephalosporins prescribed

Majority of the patients 216 (86.4%) received IV administration of cephalosporins, followed by oral route of administration, 21 (8.4%). A total of 13 (5.2 %) patients were observed to have IV to oral switch over during their stay in the hospital.

Distribution of subjects based on gastro-protective agents prescribed.

Out of total subjects enrolled, 226 (90.4%) were prescribed with gastro-protective agents. Among 226 subjects, majority 191 (84.5%) were prescribed with Pantoprazole followed by Rabeprazole, 11 (4.9%). The detailed summary is given in Table 8.

Prescribing pattern of antibiotic agents co-prescribed.

Out of 250 patients, 106 (42.4%) received a total of 121 other antibiotic agents along with cephalosporins. Azithromycin was found to be the highest prescribed, 37 (30.6%), followed by Metronidazole 24 (19.8%). Details are summarized in Table 9.

Discussion

In the current study, majority 65 (26.8%) of the subjects were found belonging to the age group of 18-29 years. Studies conducted by (Kiran *et al*., 2016; Reddy *et al*., 2015 and Naveen *et al*., 2018) reported a contradictory finding, where 26 (34.2%) belonged to 61-70 years of age, 58 (23.2%) belonged to 31-40 years and 32 (29.1%) belonged to 60 years of age and above respectively. Gender analysis revealed a predominance of male population, 132 (52.8%) over females, 118 (47.2%). Several other studies conducted by (Goudanavar *et al*., 2016; Shimels *et al*., 2015; Naveen *et al*., 2018 and Arul *et al*., 2017) also reported similar results. This may be due to the increased exposure of males to environmental trigger factors leading to various bacterial infections. Majority of the patients, 162 (64.8%) treated with cephalosporins stayed in hospital for 1-7 days followed by 8-14 days, 69 (27.6%) which was in a way related to the study conducted by (Goudanavar *et al*., 2016) which showed a higher percentage (66%) for 3-6 days, followed by 7-14 days (37%). The present study showed an average length of hospital stay of 7.04 which was comparable with the mean value obtained by (Kiran *et al*., 2016) but was in contradiction to the study conducted by (Gururaja *et al*., 2013) where the mean length of hospital stay was 13.5.

In the present study, 121 (48.4%) subjects were presented with comorbid conditions. A study conducted by (Naveen *et al*., 2018) showed 62.7% of the study subjects exhibiting comorbidities, which is found to be opposing with the present study result. Study showed a majority of hypertensive patients, 73 (45.3%), followed by Diabetes Mellitus, 49 (30.4%). This was in contradiction to the results obtained by (Arul *et al*., 2017) where majority of the subjects were found diabetic, 20 (13.33%), followed by patients with hypertension, 15 (10%).

In our study, most of the patients 67 (26.8%) were prescribed with cephalosporin antibiotics for LRTI, followed by UTI and acute gastroenteritis, 32 (12.8%) each. This was similar to a study conducted by (Dahal *et al*., 2017) where highest percentage was found with LRTI (80.66%), followed by acute gastroenteritis (7.33%). Present study results were found contradictory to the study conducted by (Jyothi *et al*., 2012) in which higher percentage was reported with UTI (16.83%). Average number of drugs prescribed among the study subjects was 8.71 which is found similar to a study conducted by (Goudanavar *et al*., 2016) whereas it was in contradiction to the study conducted by (Dahal *et al*., 2017) which showed an average value of 5.8. The use of third generation cephalosporins was found to be 100% in our study. This was similar to the study conducted by (Arul *et al*., 2017) where the use of third generation cephalosporins were found to be the highest with a value of 99.33%. Since there is not even a single 2nd generation drug prescribed, the present result is highly inconsistent with the study conducted by (Naveen *et al*., 2018) wherein second, third and fourth generation cephalosporins collectively constituted 13.6%. Out of 250 subjects, majority received Ceftriaxone, 159 (60.0%) and is highly comparable with the study conducted by (Goudanavar *et al*., 2016; Dahal S *et al*., 2017; Gururaja *et al*., 2013; Reddy *et al*., 2015; Naveen *et al*., 2018 and Arul *et al*., 2017) whereas a study conducted by (Kiran *et al*., 2016) showed Cefoperazone sodium+ sulbactam as the agent most

commonly prescribed among 38.4% of the study population which is thereby inconsistent with that of present study result.

In the current study, 205 (82.0%) prescriptions had brand drugs followed by generic drugs in 45 (18.0%). This was comparable to the result of studies conducted by (Kiran *et al*., 2016 and Naveen *et al*., 2018) which also showed a high percentage of brand drug prescription, 81.82% and 86.4% respectively. This could be a result of various promotional strategies on physicians by different pharmaceutical companies ultimately trying to achieve high market for their products. The present study showed that cephalosporins were prescribed mostly by parenteral route, 216 (86.4%) followed by oral, 21 (8.4%). This result is highly comparable to the study outcomes of (Kiran *et al.*, 2016; Dahal *et al*., 2017 and Gururaja *et al*., 2013) as they reported parenteral route of administration of cephalosporins among 86.78%, 79.33% and 69% of the total enrolled subjects.

106 (42.4%) patients were prescribed with other antibiotics along with cephalosporins. This was not consistent to the studies conducted by (Kiran *et al*., 2016 and Gururaja *et al*., 2013) which showed a report of 31.65% and 37.75% respectively. In our study, Azithromycin was prescribed among 37 (14.8%) patients followed by Metronidazole among 24 (9.6%). Studies by (Kiran *et al*., 2016 and Gururaja *et al*., 2013) showed a contradicting result as Metronidazole was found to be the most commonly co-prescribed antibiotic agent in their studies.

Conclusion

In the current study, ceftriaxone was found to be most routinely prescribed cephalosporin agent. Majority of the patients prescribed with cephalosporins were diagnosed with lower respiratory tract infection, followed by urinary tract infection and acute gastroenteritis. Drug utilization studies conducted periodically can contribute to appropriate usage of drugs, including antibiotics. The current study provides an insight to the healthcare team on the importance of rational use of antibiotic agents among the patient population.

Table 1: Age wise distribution of the study subjects

Age Group (in years)	Frequency (n)	Percentage (%)
18-29	65	26.0
30-39	21	8.4
40-49	42	16.8
50-59	39	15.6
60-69	52	20.8
>70	31	12.4
Total	250	100

Table 2: Gender and age wise distribution of study subjects

Age Group	18-29	30-39	40-49	50-59	60-69	>70	Total
Male	28	9	27	22	31	15	132
Female	37	12	15	17	21	16	118
Total	65	21	42	39	52	31	250

Table 3: Distribution of subjects based on the length of hospital stay

Length of Hospital Stay (in days)	Frequency (n)	Percentage (%)
1-7	162	64.8
8-14	69	27.6
15-21	15	6.0
22-28	4	1.6
Total	250	100

Table 4: Distribution of subjects based on their social habits

Social Habit	Frequency (n)	Percentage (%)
Alcohol	18	45.0
Alcohol+ Smoking	12	30.0
Smoking	6	15.0
Substance use	1	2.5
Alcohol+ Substance use	1	2.5
Smoking+ Substance use	1	2.5
Alcohol+ Smoking+ Substance use	1	2.5
Total	40	100

Table 5: Distribution of comorbid conditions reported

Comorbidities	Frequency (n)	Percentage (%)
Hypertension	73	45.3
Diabetes Mellitus	49	30.4
Ischemic Heart Disease	18	11.2
Dyslipidaemia	11	6.8
Asthma	5	3.1
Seizure Disorder	3	1.9
Rheumatoid Arthritis	2	1.2
Total	161	100

Table 6: Distribution of subjects based on diagnosis

Diagnosis	Frequency (n)	Percentage (%)
Lower respiratory tract infections	67	26.8
Urinary tract infection	32	12.8
Acute gastroenteritis	32	12.8
Chronic liver disease	14	5.6
Chronic kidney disease	9	3.6
Upper respiratory tract infections	9	3.6
Viral fever	8	3.2
Dengue fever	7	2.8
Enteric fever	7	2.8
NSAID induced acute kidney injury	7	2.8
Malaria	5	2.0
Acute Febrile Illness	4	1.6
Tuberculosis	4	1.6
Urinary tract infection + Acute gastroenteritis	4	1.6
Hepatitis	3	1.2
Cellulitis	3	1.2
Leptospirosis	3	1.2
Fracture	2	0.8
Leptospirosis+ Acute kidney injury	2	0.8
Urinary tract infection+ Respiratory tract infections	2	0.8
HIV infection+ Chronic kidney disease	2	0.8
Cystitis	1	0.4

Pancreatitis	1	0.4
Cholelithiasis	1	0.4
Alcoholic Liver Disease	1	0.4
Sinusitis	1	0.4
Alcohol Dependence Syndrome	1	0.4
Alcohol Withdrawal Syndrome	1	0.4
Alcohol Intoxication	1	0.4
Cerebro vascular accident with seizures	1	0.4
Cervical Lymphadenopathy	1	0.4
Myelodysplastic syndrome	1	0.4
Urinary tract infection+ Abdominal ulcer	1	0.4
Acute kidney injury+ Respiratory tract infection	1	0.4
Viral fever+ Sinusitis	1	0.4
Urinary tract infection+ Chronic liver disease	1	0.4
Leptospirosis+ Filariasis	1	0.4
Chronic kidney disease+ Respiratory tract infection	1	0.4
Chronic liver disease + Cellulitis	1	0.4
HIV infection+ Respiratory tract infection	1	0.4
Respiratory tract infection + Acute gastroenteritis	1	0.4
Acute gastroenteritis + AKI+ UTI	1	0.4
Acute gastroenteritis + LRTI+ UTI	1	0.4
Gullian Barre syndrome	1	0.4
Benign prostrate hypertrophy	1	0.4
Total	**250**	**100**

Table 7: Prescribing pattern of cephalosporins

Generation	Cephalosporin antibiotics	Frequency	Percentage (%)
I & II	NIL	0	0
III	Cefixime	22	8.3
	Cefixime+ Clavulanic acid	2	0.8
	Ceftriaxone	159	60.0
	Ceftriaxone+ Tazobactam	41	15.5
	Cefaperazone sodium+ sulbactam	27	10.1
	Cefotaxime	3	1.1
	Cefpodoxime	3	1.1
	Cefpodoxime + clavulanic acid	8	3.0
IV & V	NIL	0	0
Total		**265**	**100**

Table 8: Distribution of subjects based on gastro-protective agents prescribed

Gastro-protective agents	Frequency (n)	Percentage (%)
Pantoprazole	191	84.5
Rabeprazole	11	4.9
Pantoprazole+Domperidone	8	3.5
Ranitidine	7	3.4
Rabeprazole+ Domperidone	4	1.5
Ilaprazole	3	1.3
Pantoprazole+ Itopride	2	0.8
Total	226	100

Table 9: Prescribing pattern of antibiotic agents co-prescribed

Antibiotics co-prescribed	Frequency (n)	Percentage (%)
Azithromycin	37	30.6
Metronidazole	24	19.8
Piperacillin+ Tazobactam	12	9.9
Doxycycline	9	7.4
Levofloxacin	6	5.0
Rifaximin	5	4.1
Linezolid	5	4.1
Amoxicillin+ Clavulanic acid	5	4.1
DOTS (HRZE)	4	3.3
Ciprofloxacin	3	2.5
Meropenem	3	2.5
Norfloxacin	3	2.5
Clindamycin	1	0.8
Nitrofurantoin	1	0.8
Ofloxacin	1	0.8
Amikacin	1	0.8
Gatifloxacin	1	0.8
Total	121	100

DOTS: Direct Observed Treatment Short course; H: Isoniazid; R: Rifampicin; Z: Pyrazinamide; E: Ethambutol

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