



## **Use of Cephalosporin Type Antimicrobials in Infection Wards in Tertiary Hospital in West India**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** Antibiotic resistance is exponentially increasing worldwide. Irrational prescription of antibiotic treatment contributes to the development of antibiotic resistance. Appropriate antibiotic use is vital in reducing the mortality caused by bacterial infections. Third generation cephalosporins are now considered as the backbone of antibiotic therapy for treatment of serious infections including those in hospitalized patients. These drugs are the commonly prescribed  $\beta$ -lactam antibiotics even before culture sensitivity reports arrive. Generation of resistance has been a growing concern for all clinicians and must be avoided at all costs. This drug utilization study was undertaken to understand the growing resistance acquired by the organisms against cephalosporins caused due to the superfluous and unrestrained use of cephalosporins in the medical wards of our institution.

**Objective:** The study objectives were to assess:

- The cephalosporins generation which was most commonly prescribed
- The relevance of cephalosporins generations used in various diseases
- The shift or addition of other antimicrobials upon failure of cephalosporins treatment

**Methods:** This was an observational study done amongst 350 patients admitted in infection wards of Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune over a period of one

year between January 2019 to December 2019 after obtaining institutional ethical clearance. Data was analyzed and values were presented descriptively in number and percentage form.

**Results:** Maximum usage of third generation cephalosporin was seen with ceftriaxone being the most commonly prescribed third generation cephalosporin in parenteral form (59.43%). Gender analysis revealed that males (60.28%) were prescribed more cephalosporins as compared to females (39.71%), whereas, frequent usage was seen in the age group 61 – 70 years. Bacteriological investigations were done in only 103 (29.42%) cases following which shift or addition of other antimicrobials was seen in 13 (3.71%) cases. Metronidazole was the most frequently co-prescribed with cephalosporins.

**Conclusion:** Our study revealed extensive usage of third generation cephalosporin and the treatment regimens implemented in majority of the cases were without prior culture sensitivity test leading to irrational prescribing. Our study, along with the various other studies, would help in taking the corrective measures to curb the unnecessary use of antibiotics, and framing the guidelines for the doctors prescribing them.

*Keywords: Cephalosporins; infection wards; ceftriaxone; drug utilization; antimicrobials.*

## 1. INTRODUCTION

Increasing morbidity and mortality owing to the infectious diseases, in spite of the availability of lifesaving antibiotics, is an alarming worldwide situation of the utmost importance. Regrettably, the use of these wonder drugs has been accompanied by the rapid appearance of resistant strains [1].

Several fields of modern medicine depend on the availability of effective antibiotic drugs; chemotherapy for cancer treatment, organ transplantation, hip replacement surgery, intensive care for pre-term newborns and many other activities could not be performed without effective antibiotics. Not only the overuse of antibiotics but also the inappropriate use (inappropriate choices, inadequate dosing, poor adherence to treatment guidelines) contribute to the increase of antibiotic resistance [2].

The excessive use of expanded spectrum beta lactam antibiotics especially the third generation cephalosporins in nosocomial infections has led to the emergence of ESBLs (Extended Spectrum beta lactamases). The increasing resistance to third generation cephalosporins has raised concern regarding the prevalence and clinical implications of infections with resistant *Escherchia coli* and *Klebshiella spp.* which are the most important production sources of ESBLs. The association between ESBL mediated infections in third generation cephalosporins use emphasizes drug utilization to optimize their use. Acknowledging the same, formulary intervention through the reduction in the usage of cephalosporins and replacing it by other antibiotic classes such as beta lactam/beta lactam inhibitor combinations as first line

empirical therapy has shown to result in decrease in rate of multidrug resistance bacteria [3].

This study was undertaken to understand the growing resistance acquired by the organisms against cephalosporins due to their unrestrained use.

## 2. MATERIALS AND METHODS

This observational study was conducted in Maharashtra, India after obtaining ethical clearance (IESC/PGS/2018/65) from Research and Recognition Committee under the Faculty of Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune, from January 2019 to December 2019 with a sample size of 350.

### 2.1 Eligibility Criteria

#### Inclusion criteria:

- Patients upto 70 years of age
- Patients who were prescribed cephalosporins
- Patients of either gender

#### Exclusion criteria:

- Patients who were not prescribed cephalosporins
- Patients with known H/O of allergy to cephalosporins

#### Evaluation parameters:

Medical case record sheets of the patients were reviewed on the basis of the following points:

- Distribution pattern of various generations of cephalosporins in patients
- Distribution pattern seen in different age groups
- Patients who do not respond to cephalosporins treatment and have been shifted to different antibiotics
- Appropriate use of cephalosporins in specific medical conditions

bacterial infections. Maximum cases, 90 (25.71%) were observed in the age group of 61 – 70 years, as the geriatric patients are more prone to be sick and have serious illness; and least cases, 20 (5.71%) were seen in up to 10 years age group.

## 2.2 Recruitment of Study Subject

All cases taking cephalosporin antibiotics and seeking care in Dr. D.Y. Patil Hospital, full filling the above mentioned criteria were considered for inclusion in the study. Cases giving consent were recruited consecutively till the desired sample size was achieved.

Table 2 shows that in 247 cases (72.57%), brand name was preferred and the most common route of administration was parenteral seen in 203 (57.43%) cases. The most likely reason for higher parenteral route of administration was the unwillingness of the patient to stay in the hospital once the parenteral drug had been stopped and also the belief of patients about the faster onset of action of parenteral as compared to the oral route. Bacteriological investigations were carried out in only 107 (30.57%) cases and not done in majority 243(69.42%) cases. This was due to the delay in obtaining the sensitivity reports which took an average of 3 days, as a result of which; antibiotic treatment was started before the test results arrived.

## 2.3 Statistical Analysis

Data was collected and entered in Microsoft Excel and analysis was done using WinPepi software (Version 11.65) and the sample size was 350. Categorical variable was expressed in terms of frequency and percentage and graphs were prepared using Microsoft excel sheet.

In cases where bacteriological investigations were done, the growth was observed only in 52 out of 107 cases (Table 1). The common organisms isolated were Escherichia coli (39 cases), Klebsiella pneumonia (6 cases), Staphylococcus aureus (3 cases), Citrobacter species (2 cases) and Methicillin and Coagulase positive staphylococcus (2 cases).

## 3. OBSERVATIONS AND RESULTS

Total 350 prescriptions were analyzed to study their prescribing patterns and observations of the same are as follows:

### 1. Distribution of cases according to gender, age and prescribing parameters

Out of total 350 cases, 211 (60.28%) were males whereas, 139 (39.71%) were females as shown in Table 1. Male preponderance was observed which may be due to the increased exposure of males to the environmental triggers and accidents, which may be the cause of various

### 2. Indications of Cephalosporins

Table 3 shows the various indications of cephalosporins. Out of the 350 cases, maximum usage was seen in 97 cases (16.57%) for LRTIs (lower respiratory tract infections), followed by 61 cases (10%) for UTIs (urinary tract infections) and least usage seen in 12 cases (2 %) of meningitis.

**Table 1. Age wise distribution of cases**

Age group	General medicine	Total (%)
0 to 10	20	5.7
11 to 20	50	14.28
21 to 30	50	14.28
31 to 40	40	11.4
41 to 50	45	12.8
51 to 60	55	15.71
61 to70	90	25.71
<b>TOTAL</b>	<b>350</b>	<b>100</b>

**Table 2. Distribution of cases according to prescribing parameters**

Characteristics	Number	Percentage
Brand name	247	72.57
Generic name	103	27.43
<b>Route of administration</b>		
Oral	147	42.57
Parenteral	203	57.43
<b>Bacteriological investigations</b>		
Done	107	30.57
Not done	243	69.42

**Table 3. Indications of cephalosporins**

Sr. No.	Indication	Number	Percentage
1.	LRTI (Lower Respiratory Tract Infection)	97	16.57
2.	UTI (Urinary Tract Infection)	61	10
3.	Fever (Temp. > 37.2 °C)	83	15.71
4.	Typhoid	13	3.71
5.	Skin and soft tissue infection	16	3.43
6.	AGE (Acute Gastro-enteritis)	47	9.43
7.	Meningitis	12	2
8.	Other	21	3.71

**3. Combinations of cephalosporins and antimicrobials co-prescribed**

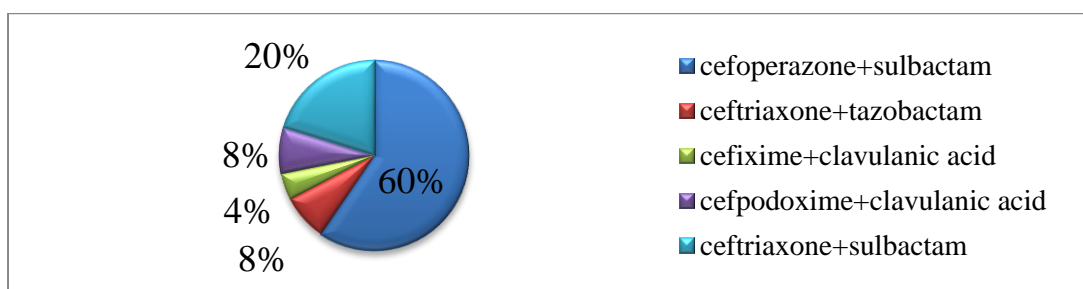
Fig. 1 gives an idea about the most commonly prescribed combination, cefoperazone with sulbactam; which is a beta lactamase inhibitor, seen in 60% of the cases. The other antimicrobials were prescribed for a broader spectrum of action against various gram positive and gram negative organisms. The frequently co-prescribed drugs were metronidazole (31%), followed by gentamicin (28%) and the least one being clindamycin in 17% cases.

**4. Generation Wise Distribution of Cephalosporins**

Table 4 shows the generation wise distribution of cephalosporins and it was observed that usage of third generation cephalosporins was predominant as seen in 216 (61.71%) cases and least use seen with fourth generation cephalosporins seen in 27 (7.71%) cases. The wide usage of third generation cephalosporins was evident due to their broad spectrum of action against both gram positive and gram negative organisms.

**Table 4. Generation wise distribution of cases**

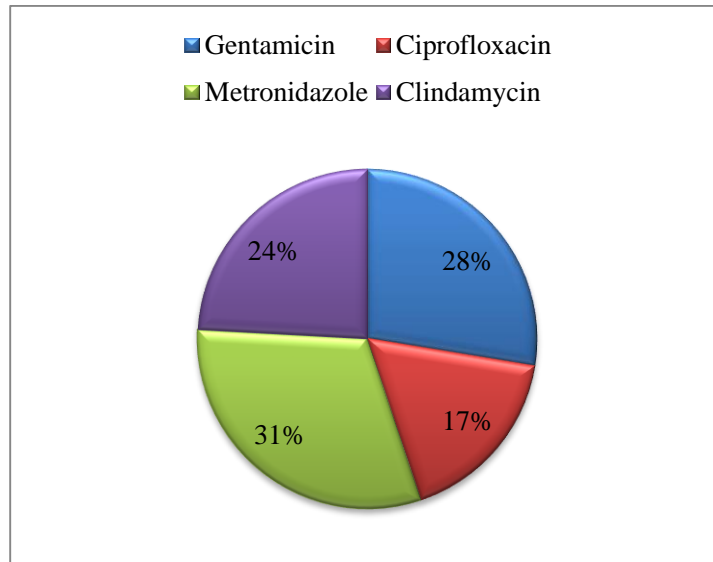
Generation	No.	%
1 <sup>st</sup> Generation	32	9.14
2 <sup>nd</sup> Generation	75	21.42
3 <sup>rd</sup> Generation	216	61.71
4 <sup>th</sup> Generation	27	7.71
<b>Total</b>	<b>350</b>	



**Fig. 1. Combinations of cephalosporins prescribed**

**Table 5. Shift to or addition of other antimicrobials**

Sr. No.	Condition	Antimicrobial culture sensitivity		Empirical Treatment	Second line Treatment	Rationale of use		No.	%
		Sensitivity	Resistant			Rational	Irrational		
1	LRTI	3	10	Ceftriaxone/ Cefotaxime	Added along Azithromycin	4	9	13	26
2	UTI		7	Cefoperazone+ Sulbactam	Shifted to Meropenem		7	7	14
3	Meningitis		3	Ceftriaxone/ Cefixime/ Cefepime	Shifted to Meropenem + Vancomycin	2	1	3	6
4	Fever	4	7	Cefuroxime/Cefixime	Added along Ceftriaxone+ Sulbactam	3	8	11	22
5	Skin and soft tissue infection		1	Cefaclor	Shifted to Ceftriaxone +Clindamycin	1		1	2
6	Typhoid		1	Cefixime	Shifted to Ceftriaxone		1	1	2
	<b>Total</b>	<b>7</b>	<b>29</b>			<b>10</b>	<b>26</b>	<b>36</b>	<b>10</b>



**Fig. 2. Antimicrobials co-prescribed with cephalosporins**

#### 5. Shift or addition of other antimicrobial agents

Table 5 shows that in 10.28% cases (36), cephalosporins were started as empirical treatment but additional antimicrobial agents had to be added along with them. A different class of antimicrobial agent had to be started for better response in some cases. Out of these cases, 7 cases showed sensitivity and 29 cases showed resistance to respective group of antimicrobials tested according to the diseases. According to the rationale of their use, most of the cases (26) showed irrationality in their use according to the hospital antibiotic policy and rational use was seen in only 10 out of the 36 cases.

#### 4. DISCUSSION

Cephalosporins are the most widely used class of antibiotics that need careful monitoring to ensure their rational use in this era where there is an increased threat due to the microbial resistance [4].

A total of 350 prescriptions were analyzed for various factors like demographic profile including the age and gender of the patients, commonly preferred route of administration, preference over brand and generic names of drugs, various indications, combinations and co-prescribed drugs and generation wise usage of cephalosporins.

There was a preponderance of those in 60 – 70 years age group (25.71%) and our results were

similar to the study conducted by Shankar PR et al. [5] where, 51.20% were above the age of 59 years. This factor influences the antibiotic prescribing, as elderly patients are more prone to have serious health issues. In our study, male preponderance (60.29%) was observed as compared to female cases (39.71%) which was in accordance to a study conducted by Kiran B et al. [6]. Male preponderance was observed which may be due to the increased exposure of males to the environmental triggers and accidents, which may be the cause of various bacterial infections.

Parenteral administration of cephalosporins was higher, 59.43% as compared to oral route of administration. The results of our study were high as compared to the standards recommended by WHO (13.4%-24.1%). [7] The most likely reason for higher parenteral route of administration was the unwillingness of the patient to stay in the hospital once the parenteral drug had been stopped and also the belief of patients about the efficacy and faster onset of action of parenteral as compared to the oral route.

In 247 cases (72.57%), brand name was preferred as compared 27.43% cases where drugs were prescribed by their generic names. A study conducted by Kiran B et al. [6] found that 18.8% drugs were prescribed by their generic name and remaining 81.82% were in brand names. Generic prescribing aides the hospital pharmacy in having a better inventory control and avoids any confusion while dispensing at the

pharmacists end. Also, generic drugs are more cost – effective than the brand drugs.

In our study, third generation cephalosporins have been widely used for lower respiratory tract infections (LRTIs) which was similar to a study conducted by Sileshi et al. [8], where LRTIs were the most common indication observed in 35% of the cases. Similar results were seen in a study conducted by Marion B et al. [9]. The frequently co-prescribed drugs were metronidazole, gentamicin and clindamycin.

In our study, the most commonly prescribed combination of cephalosporins was that of cefoperazone with sulbactam followed by ceftriaxone with sulbactam. A study conducted by Goudanavar P et al. [10] showed higher use of the combination ceftriaxone & sulbactam followed by cefoperazone & sulbactam.

Our study showed high usage of cephalosporins with the third generation predominant in 216 cases (61.71%). Another similar study conducted by Marion B et al. [9] shows higher usage of 3GCs (95.85%), whereas a study conducted in a teaching hospital in Nepal shows a low use of 3GCs.

The antimicrobial culture sensitivity test was done in 30.57 % cases only when resistance towards the given antibiotic was suspected or presence of severe infection. *E. coli* was the most frequently documented organism upon culture sensitivity test. In cases where bacteriological investigations were done, the growth was observed only in 52 out of 107 cases (Table 1). The most common organism isolated was *Escherichia coli* (39 cases) followed by *Klebsiella pneumonia* (6 cases). This was similar to the study done by Soman N et al. [11].

Our study showed lack of abidance to the hospital antibiotic policy [12] (For empiric as well as definitive therapy) of Dr. D. Y. Patil Medical College, Hospital and Research Centre. This was probably due to lack of availability of the antimicrobial agents and delay in obtaining the antimicrobial culture sensitivity reports. It was seen that 36 (10.28%) cases had to be shifted to other antimicrobial treatment, either along with cephalosporin or with another group of antimicrobials. Out of these cases, 7 cases showed positive culture sensitivity and 29 cases showed resistance to respective group of antimicrobials tested according to the

diseases. The treatment regimens implemented in most of the cases (26) showed irrationality in their use according to the hospital antibiotic policy and rational use was seen in only 10 out of the 36 cases.

## 5. CONCLUSION

Third generation cephalosporins were the most widely used antimicrobial agents in our study without prior culture sensitivity testing which led to irrationality of the prescription. The sample size in the present study might not be sufficient to represent the overall prescribing pattern for which repeated prescription audit is necessary to assess the changes in the prescribing behaviours. Revising the ongoing antibiotic prescribing practices demands robust infection control interventions, strict implementation of antibiotic policies along with appropriate education and laboratory support. Further similar type of studies need to be conducted to emphasize the rationality of use of cephalosporins and thereby also help in reducing the trend of growing resistance to antibiotics.

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## DISCLAIMER

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

## ETHICAL APPROVAL

Ethical clearance (IESC/PGS/2018/65) is obtained from Research and Recognition Committee under the Faculty of Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune.

## CONSENT

Cases giving consent were recruited consecutively till the desired sample size was achieved.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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