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ORIGINAL ARTICLE

Drug Utilization Studies of Empirically Prescribed Antimicrobial Agents in Surgical Patients of a Tertiary Care Hospital in Maharashtra, India: An Observational Study

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Abstract

Introduction: Antibiotic resistance, a threat to the public health, is rapidly increasing worldwide. Irrational and unnecessary antibiotic treatment, contributes to the development of antibiotic resistance. Third-generation cephalosporins are considered the backbone of antibiotic therapy for the treatment of different serious infections, including those in the hospitalized patients. Resistance to them has been increasing rapidly. This drug utilization study was undertaken to understand the growing resistance acquired by the organisms against cephalosporins caused due to the rampant use of cephalosporins in the surgical wards of our institution.

Method: This was an observational study done amongst 350 patients admitted in General Surgery, Orthopedics, Obstetrics & Gynecology and Otorhinolaryngology wards of Dr. D. Y. Patil Medical College and Hospital, Pimpri, Pune over a period of one year between January 2019 to December 2019 after obtaining ethical clearance. Appropriateness was assessed with the help of modified Kunin's criteria. Data was analyzed and values were presented descriptively in number and percentage form.

Results: Maximum usage of cephalosporins, 40.28% was seen in the General Surgery ward with ceftriaxone (30.28%) 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.

Key words: Cephalosporins, General surgery, ceftriaxone, drug utilization, antimicrobials

Introduction

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

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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].

Third-generation cephalosporins are considered the backbone of antibiotic therapy for the treatment of different serious infections, including those in the hospitalized patients [3]. Resistance to cephalosporins, especially the

3rd and 4th generation cephalosporins, has increased because of plasmid-encoded or chromosomal â-lactamase. Resistance also occurs when there is decreased penetration of the drug as a result of alterations to the outer membrane proteins, or mutations of the binding-site proteins [4].

The economic and health consequences are already being felt by the world as the crucial medicines are becoming ineffective. The economic and health consequences are already being felt by the world as the crucial medicines are becoming ineffective [5].

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

This study was designed to study the drug utilization pattern of cephalosporins seen in the surgical wards of our institution with the objectives of the cephalosporin generation which is most commonly prescribed and the shift or addition of other antimicrobials upon failure of cephalosporins treatment.

Material & Method

This observational study was conducted in a tertiary care hospital in Maharashtra, Indiaafter obtaining ethical clearance, from January 2019 to December 2019 with a sample size of 350 from departments of General Surgery, Orthopedics, Obstetrics & Gynecology and Otorhinolaryngology. Patients upto 70 years of age of either gender, who were prescribed cephalosporins were included in the study, while those with known history of allergy to cephalosporins were excluded.

Drug utilization of cephalosporins were categorized according to age, gender, cephalosporin generation commonly prescribed, route of administration, name, indication wise use, combinations of cephalosporins used, co-prescribed drugs, bacteriological investigations and the shift or addition of other antimicrobial agents. Rationality of prescriptions was analyzed on the basis of modified Kunin's criteria [6].

I. Agree with use of therapy given as in the prescription. The treatment is appropriate in terms of choice of drug, dose, dosage regimen, and duration of therapy.

II. Agree with use of therapy but a potentially fatal infection cannot be ruled out.

III. Agree with use of therapy but a different (usually less expensive and toxic) combination of therapy is preferred.

IV. Agree with use of therapy but a modified dose, dosage regimen, and duration would be recommended.

V. Disagree with use of therapy; administration is unjustified or unnecessary use of drugs.

These indicators help facilitate quick and reliable assessment of drug use in health care.

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

Observations and Results

Total 350 prescriptions were analyzed to study their prescribing patterns. The observations of this study are as follows:

1. Distribution of cases according to gender and age in various departments:

Out of total 350 cases, 211 (60.28%) were males and 139 (39.71%) were females. Among 350 cases, a maximum of 71 i.e. 20.28% of the total cases were in the age group of 61 – 70 years seen in the General Surgery and the least number of cases were observed in the age group of 0 – 10, i.e. 19 (5.42%) cases in Obstetrics & Gynecology ward.

2. Distribution of cases according to prescribing parameters:

Table 2 shows the distribution of cases according to prescribing parameters. Out of total 350 cases, it was seen that in majority of the cases, 247 (70.57%), brand name was preferred over generic names which was prescribed in 103 (29.43%) cases. The most common route of administration was parenteral as seen in 208 (59.43%) cases as compared to oral route seen in 142 (40.57%) cases. Bacteriological investigations were carried out in only 103 (29.42%) cases and not done in majority, i.e. 247 (70.57%) cases.

3. Indications of cephalosporins:

Table 3 shows the various indications of cephalosporins. Out of the 350 cases, maximum usage was seen in 77 cases (22%) for surgical prophylaxis, followed by 69 cases (19.71%) in trauma and least seen in 31 cases (8.85%) of abscess.

4. Combinations of cephalosporins prescribed:

Figure 1 shows the various combinations of cephalosporins prescribed. It was seen that majority of the cases, 60%, were prescribed cefoperazone with sulbactam combination, which was followed by 20% prescriptions having ceftriaxone with sulbactam combination. Least common was the

Table 1: Age wise distribution of cases in various departments

AGE GROUP	GENERAL SURGERY	OBGY	ORTHO	ENT	TOTAL (%)
0 to 10	6	1	2	10	5.42
11 to 20	14	5	8	16	12.28
21 to 30	15	15	6	9	12.85
31 to 40	18	21	9	8	16
41 to 50	18	15	10	11	15.42
51 to 60	30	8	17	7	17.71
61 to70	40	11	15	5	20.28
TOTAL	141	76	67	66	100

Table 2: Distribution of cases according to prescribing parameters

Characteristics	**Number**	**Percentage**
Brand name	247	70.57
Generic name	103	29.43
Route of administration		
Oral	142	40.57
Parenteral	208	59.43
Bacteriological investigations		
Done	103	29.42
Not done	247	70.57

Table 3: Indications of cephalosporins

Indication	Number (%)
Trauma	69 (19.71%)
Abscess	31 (8.85%)
Diabetic foot ulcer	38 (10.85%)
Surgical prophylaxis	77 (22%)
Intra abdominal conditions	53 (15.14%)
Cellulitis	39 (11.14%)
Infections	43 (12.28%)

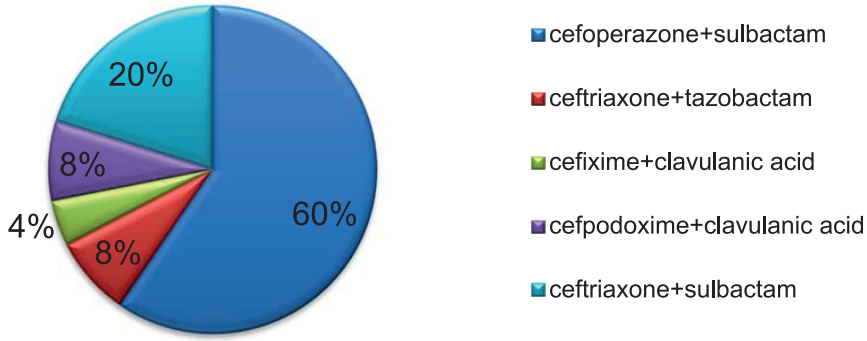

Figure 1: Empirically prescribed antimicrobial agents

Table 4: Shift or addition of other antimicrobial agents

Sr. No.	Condition	Empirical treatment	Second line treatment	Number (%)
1.	Intra abdominal	Ceftriaxone/ Cefoperazone/ Cefotaxime	Shifted to Meropenem	7 (14%)
2.	Abscess	Cefpodoxime/ Cefuroxime	Shifted to Cefoperazone+Sulbactam	3 (6%)
3.	Trauma	Ceftriaxone/ Cefotaxime	Shifted to Meropenem	2 (4%)
4.	Skin and soft tissue infection	Cefaclor	Shifted to Ceftriaxone+Clindamycin	1 (2%)
	Total			13 (3.71 %)

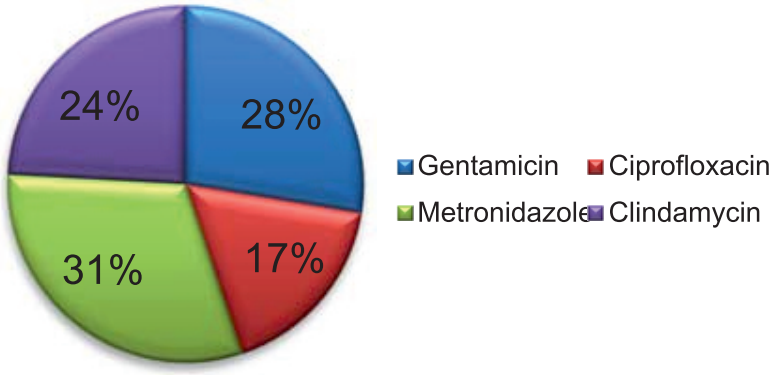

Figure 2: Antimicrobials co prescribed with cephalosporins

combination of cefixime with clavulanic acid, seen in just 4% of the prescriptions analyzed.

5. **Antimicrobials co–prescribed with cephalosporins:**

   Figure 2 shows the commonly co–prescribed antimicrobials with cephalosporins. It was observed that the most commonly co–prescribed drugs were metronidazole (31%), followed by gentamicin (28%) and clindamycin (24%).

6. **Shift or addition of other antimicrobial agents:**

   Table 4 shows that in 3% cases (13), cephalosporins were started as empirical treatment but additional antimicrobial agents had to be used along with them. In some cases, a different class of antimicrobial agent had to be started for better response.

Discussion

Drug utilization research was defined by WHO in 1997, as "the studies of marketing, distribution, prescription and use of drugs in a society, giving special emphasis on the resulting medical, social and economic consequences" [7].

Antibiotic resistance among the pathogenic microorganisms is a matter of worldwide concern. The most important driving force for the development of such resistance is selective pressure by the antimicrobial drugs. The most commonly prescribed drugs in hospitals are antimicrobial agents and in developed countries, around 30% of the hospitalized patients are treated with these drugs [8].

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 [9].

In our study, a total of 350 prescriptions were reviewed and analyzed to study the cephalosporin prescription pattern in our hospital. Various factors were taken into consideration; demographic profile including the age and gender of the patients, prescription pattern according to the generation of cephalosporins commonly prescribed, the commonly preferred route of administration, the various indications and whether the brand or generic

names of drugs are more preferred.

In the present study, among the patients admitted to the various wards and ICU of various departments, namely, General Surgery, Medicine, Obstetrics & Gynecology, Otorhinolaryngology, Orthopaedics and Pediatrics, there was a preponderance of those of or above the age of 60 years (24%), as is depicted in Table 1. This factor may have influenced the antibiotic prescribing, as older patients are more prone to be sick and have serious health issues. This was similar to the results of a study conducted by Shankar PR et al. (2003) [10], where, 51.20% were above the age of 59 years.

Gender wise, in our study we saw a male preponderance (60.29%) more than the females (39.71%). This was similar to a study conducted by Kiran B et al. (2016) [11], where, among the 115 prescriptions, 76 were males and rest 39 were females. Male preponderance, mostly in the elderly may be due to the increased exposure of males to the environmental triggers, which may be the cause of various bacterial infections. These results were similar to those obtained from various other studies [9, 12].

The study showed high usage of cephalosporins with the third generation cephalosporins (61.14%) being used in majority of the wards. This was followed by second generation cephalosporins (19.71%). Out of the third generation cephalosporins, ceftriaxone was most commonly prescribed. Another similar study conducted by Marion B et al. (2002) shows higher usage of 3GCs (95.85%), whereas a study conducted in a teaching hospital in Nepal shows a low use of 3GCs [10,13]. This higher use may be due to its broad spectrum of activity against most of the bacterial species responsible for causing infections, especially against the gram-negative microorganisms, as well as the routine availability of these drugs. Their rapid use in the hospital settings to treat various infections has increased, exerting a significant influence over the rates of multidrug-resistant nosocomial pathogens.

In total 350 patients' prescriptions, 103 prescriptions were prescribed by generic names (29.43%) and the rest 247 were prescribed by brand names (70.57%). A study conducted by Kiran B et al (2016) [11] found that 18.8% drugs were prescribed by their generic name and the remaining 81.82% were in brand names.

In our study, parenteral administration of cephalosporins was higher, 59.43% as compared to 40.57% seen with oral administration. The results of our study were high as compared to the standards recommended by WHO (13.4%-24.1%) [14]. The possible reasons for the high use of parenteral can be the unwillingness of patient to stay in the hospital once the parenteral drugs had been stopped, and belief of the patients about the efficacy and faster onset of action of parenteral as compared to oral.

It was found that the most common indication for cephalosporins administration was for surgical prophylaxis. As per Kunin's modified criteria, 77% of patients received cephalosporins therapy appropriately, while 23% received inappropriately. In our study, it was observed that bacteriological investigations were done in only 29.42% of the patients. In majority of the patients, antibiotic treatment was started without prior bacteriological testing; this was evident in 70.57% of the cases. Prior to the initiation of any antibiotic treatment, the culture sensitivity test was not routinely performed in our hospital. The reasons were probably due to the delay in obtaining the sensitivity reports which took an average of 3 days, which was not possible in the cases requiring urgent treatment with broad spectrum antibiotics so as to cover most of the organisms in the gram-positive and gram-negative group and the economic burden on patient. The antimicrobial culture sensitivity test was done only when the patient was suspected of resistance towards an antibiotic or in case of severe infection. E. coli was the most frequently documented organism upon culture sensitivity test. This was similar to the study done by Soman N et al. (2019) [15].

In our hospital, third generation cephalosporins have been widely used for surgical prophylaxis. For surgical prophylaxis, third generation cephalosporins, such as ceftriaxone, cefotaxime, cefoperazone, ceftazidime or ceftizoxime are usually not recommended. The medical community has accepted this despite these recommendations and are currently used in many countries as the most common drugs in surgical prophylaxis [16].

A study conducted by Soman N et al. (2019) [15], it was seen that 51.6% were found to be compliant for an overall evaluation of indication, dose, frequency and duration of treatment according to the antibiotic policy. 28.4% cases non-complying to the policy were related to the differences in indication, dose, route, frequency and duration of administration between practice and the policy. According to our hospital antibiotic policy, antibiotic prophylaxis should not continue for more than 24 hrs, and does not recommend an additional dose be administered post-operatively. This was not abided to in most of the cases which could have led to ineffective response and use of higher antimicrobials. This could possibly be due to the time required to get results for the antibiotic sensitivity tests which take around 24-72 hours [17].

In our study, it was seen that ceftriaxone was the most commonly prescribed amongst the third generation cephalosporins, either alone or co–prescribed with other antibiotics. Metronidazole (31%) was the most commonly co–prescribed antimicrobial agent followed by gentamicin

(28%) and clindamycin (24%).

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. (2016) [18] showed higher use of the combination ceftriaxone and sulbactam followed by cefoperazone and sulbactam.

It was seen that 13 (3%) cases had to be shifted to other antimicrobial treatment, either along with cephalosporin or with another group of antimicrobials. For empiric or the first line treatment, most commonly used cephalosporin was ceftriaxone. In some cases, a different class of antimicrobial agent had to be started for better response. This was in accordance with a study conducted by Hwang KP et al (2009) [19] that revealed that ceftriaxone had high activity against the most common pathogens isolated thereby being used frequently.

Conclusion

Based on the findings of our study, it was concluded that there was extensive use of cephalosporins, especially the third generation cephalosporins. Ceftriaxone was found to be the most widely used amongst all others belonging to this class.

It was also evident that majority of the treatment regimens implemented in our hospital were without prior culture sensitivity testing. This led to the irrationality of the prescription. Some of the possible reasons for inappropriate use are lack of availability of alternative antibiotics, the cost of the healthcare and the drug supply being inconsistent majority of the times.

In order to achieve optimal compliance to the antibiotic policy formulated by the hospital so as to reduce the emergence of resistant strains and irrational use, it is recommended that there is strict compliance to the guidelines. To ensure the same, periodic surveillance of the same is required in order to achieve the rational use of cephalosporins. This practice would further assist in optimizing the clinical care of patients provided by the clinicians. The number of cases in the present study might not be sufficient to represent the overall prescribing pattern where the repeated prescription audit is necessary to assess the changes in the prescribing behaviour. Further similar type of studies should be conducted to emphasize the rationality of the use of cephalosporins and thereby do the appropriate changes in the antibiotic policy for the same.

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References

1. Davies J, Davies D. Origins and Evolution of Antibiotic Resistance. Microbiol Mol Biol Rev 2010;74(3):417–433.
2. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon. Pathog Glob Health. 2015;109(7):309-318.
3. Segreti J, Levin S. Bacteriologic and clinical applications of a new extended-spectrum parenteral cephalosporin. Am J Med. 1996;100(6):45S–51S
4. High levels of antibiotic resistance found worldwide [Internet]. 2018 Jan 29[cited2018 Jul 18]. Available from: http://www.who.int/mediacentre/news/releases/2018/antibiotic-resistance-found/en
5. International organizations unite on critical recommendations to combat drug-resistant infections and prevent staggering number of deaths each year. [Internet]. 2019 Apr 29[cited 2019 Dec 21].Available from: https://www.who.int/news-room/detail/29-04-2019-new-report-calls-for-urgent-action-to-avert-antimicrobial-resistance-crisis
6. Kunin CM. Rational use of antibiotics. WHO Drug Inf. 1990;4(1):4-7.
7. WHO Expert Committee. Introduction to drug utilization research, World Health Organization: Geneva, 2003. Accessed on 27-07-2019.
8. JWM Van der Meer. Quality of antimicrobial drug prescription in hospital. Clin Microbiol Infect. 2001;7(6):12-15.
9. Laxminarayan R, Duse A, Wattal C, Zaidi AK, Wertheim HF, Sumpradit N, et al. Antibiotic resistance the need for global solutions. The Lancet Infect Dis. 2013;13(12):1057-98.
10. Shankar PR, Partha P, Shenoy NK, Easow JM, Narayanan K. Prescribing patterns of antibiotics and sensitivity patterns of common microorganisms in the Internal Medicine ward of a teaching hospital in Western Nepal: a prospective study. Ann Clin Microbiol Antimicrob. 2003;2(1):7.
11. Kiran B, Ghufran MA, Kumar TSS, Kumar DS. The drug utilization of cephalosporins in a tertiary care hospital. World J Pharm PharmSci Dec 2016;5:1201-16.
12. Gururaja MP, Sarah A, Samaga L, Joshi H, Nair S, Shastry CS. Cephalosporin utilization evaluation in a university teaching hospital: prospective study. J Drug Deliv Therapeut. 2013;3(2):83-7.
13. Marion B, Tony MK, Jonathan GA. Ceftriaxone and cefotaxime use in Victorian hospitals. Med J Aust. 2002;176(11):524-9.

14. Vooss AT, Diefenthaeler HS. Evaluation of prescription indicators established by the WHO in Getulio Vargas - RS. Braz J Pham Sci.2011;47(2):385-90.

15. Soman N, Panda BK, Banerjee JK, John SM. A study on prescribing pattern of cephalosporins utilization and its compliance towards the hospital antibiotic policy in surgery ward of a tertiary care teaching hospital in India. Int Surg J. 2019;6(10):3614- 3621.

16. Geroulanos S, Marathias K, Kriaras J, Kadas B. [Review] Cephalosporins in surgical prophylaxis. J Chemother. 2001;13(1):23-6.

17. Hospital Antibiotic Policy. Dr. D. Y. Patil Medical College, Hospital & Research Center, Pune. Available from: https://medical.dpu.edu.in/ANTIBIOTIC-POLICY-DYPMCH.aspx Accessed on 15 September 2019.

18. Goudanavar P, Panavila L, Ninan N, Pratima KC. Drug use evaluation of third generation cephalosporins in tertiary care hospital. Int J Ther App. 2016;32:81-85.

19. Hwang KP, Tang YF, Shen YH. Activity of ertapenem, ciprofloxacin, ceftriaxone, piperacillin-tazobactam, and ampicillin-sulbactam against 12 common clinical isolates of community-acquired bacteremia. J Microbiol Immunol Infect. 2009;42(5):433-8.