

DRUG UTILIZATION EVALUATION OF CEPHALOSPORINS IN GENERAL MEDICINE UNITS OF RURAL TERTIARY CARE HOSPITAL

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ABSTRACT

Antibiotics are valuable discoveries of modern medicine and their use has led to a decline in the morbidity and mortality associated with various infectious diseases. As bacterial resistance has grown due to the increasing use of antibiotics, we sought to evaluate the current utilization of cephalosporins in in-patients of medicine department of tertiary care hospital. This was a prospective observational study carried out for in-patients in medicine departments. The documented data were evaluated for use, safety outcomes and cost for the treatment associated with the use of cephalosporins. One hundred and one patients were identified for the use of cephalosporins. Cephalosporins usage accounted for 30.02% of total admission. Male patients accounted for 50.50% while female patients were 49.50%. The average length of hospital stay was 7 days. Co-morbid condition is accounted for 24.88%. 74.26% patients received cephalosporins for empirical therapy whereas 25.74% received for specific treatment. Majority of hospitalized patients had UTI (16.83%) followed by GI (14.85%) as primary diseases. The widely prescribed cephalosporin was ceftriaxone 48.51%. Majority of hospitalized patients received injection 81.18% and oral 18.82% of cephalosporins. A total of 9 adverse drug reactions were identified. The average direct cost incurred per patient was Rs 1047.90. Cephalosporins cost accounted for 74.21% of the total medication expenses (Rs 2333469.68). Cephalosporins especially third generation were widely used in medicine departments to treat various disease conditions. Urinary tract Infections is the major disease condition followed by Respiratory Tract Infections and Digestive system infections were seen in the admitted patients. Antibiotics usage cost is accounted for 70% of total hospital stay.

Keywords: Cephalosporins, Drug Utilization Evaluation, Adverse Drug Reactions, Direct cost

INTRODUCTION

According to WHO Drug utilization is defined as the "marketing, distribution, prescription, and use of drug in a society, with special emphasis on the resulting medical, social and economic consequences."¹

Drug Utilization Evaluation (DUE) has been defined by the American Society of Health System Pharmacists (ASHP) as a "Criteria-based, ongoing, planning and systemic process for monitoring and evaluating the prophylactic, therapeutic and empiric use of drugs to help, assure that they were provided appropriately, safely and effectively."^{2,3}

Drug therapy is considered to be major component of patient management in healthcare setting, including primary healthcare. Although the benefit patients gain from pharmacological intervention are valuable, the risks of drugs and consequences of inappropriate use cannot be overlooked.⁴ The introduction of potent drugs with an increased incidence of adverse drug reactions, the cost of medication, and focus on drug use outcomes and the clinical misuse of drugs may result in preventable patient morbidity and mortality, costly remedial care, additional cost for diagnosis and management of iatrogenic disease and unnecessary wastage of health resources. In recognition to this problem DUE has been recommended as a method for identifying inappropriate or unnecessary drug use, it monitor, evaluate and promote rational drug therapy.^{5,6,7}

DUE is a method by which information is retrieved to identify problems of drug use and also serves as a means to rectify the problem, thereby contributing to rational drug therapy.⁸ DUE examines the process of drug administration, dispensing, outcomes of treatment, thereby helping the health care system to realize, interpret and ameliorate the prescribing, administration and utilization of medication.⁷

Clinician often prescribe three or four drugs to treat the most trivial conditions for the sake of satisfying the patients need to receive drugs or the drug sellers need for profit. Inadequate knowledge of treatment regimens, lack of diagnostic competence have contributed to incorrect drug choice, incorrect dose, adverse drug reactions, drug interactions, and use of more

expensive drugs when less expensive drugs would be equally or more effective.⁹

DUE studies are required for all drugs in general and particularly for antibiotics because use of antibiotics in hospitals account for 20% to 50% of drug expenditures.^{10,11}

MATERIAL AND METHOD

This was a prospective cross sectional and interventional study was conducted in the paediatric department of Adichunchanagiri Hospital and Research Center; B G Nagara, for a period of 9 months. Ethical committee clearance was obtained on 22/6/2010 (Ref: AIMS/EC/601/2010-11 from Adichunchanagiri Hospital and Research Center).

Study criteria

This study criterion was the in-patients of medicine department who were treated with cephalosporins.

Source of data

Patient data relevant to the study was obtained from the following sources

Inpatients: Patient case records, medication charts and lab reports

Outpatients: Prescriptions

Material used

A well designed patient data collection form was developed and used for this study. The data collection form was developed by consulting physicians and staffs of pharmacy practice department.

Study procedure

Patients were enrolled into study based on study criteria. The cases which had found with cephalosporins in the case records and the full details of the cases including patient name, sex, age, laboratory investigations and other details brought in to the self designed patient data collection form. All the enrolled patients were monitored from the date of admission until discharge for

any change in the drug therapy. The data was entered in Microsoft access sheet for easy reference and analysis of results later. Criteria for evaluation includes appropriateness of drug of choice for indication, dose, frequency of the drug administration, duration of the therapy, drug interactions and adverse drug reactions of cephalosporins will be evaluated. The entire data was analyzed by using different statistical methods in consultation with bio statistician.

RESULTS

Out of 101 patients from medicine department 50.50% (n=51) were male and 49.50% (n=50) were female. The average ages of male and female patients were 41.98 and 40.02 years respectively. Majority of patients belonged to age group of 51-60.

Gender distribution of patients

Out of 101 Patients male were 51 and female patients were 50. Male patients are significantly more

Co-morbid condition of Study patients

Out of 101 patients enrolled in the study 75.25% patients did not have any co morbid conditions. Whereas 24.75% patients had one and two co morbid conditions.

Type of treatment during hospital stay

In our study more no of patients received empirical therapy 74.26% and patients 25.74% only received specific therapy of treatment.

Site of infection during hospital admission of study patients (n=101)

Majority of patients admitted to the medicine department due to Urinary tract infections 16.83% followed by Gastrointestinal diseases 14.85% and Lower respiratory tract diseases 12.87% as the primary disease conditions.

Therapeutic class of medication used during hospital stay (n=101)

The most therapeutic class of drugs used during hospital stay was antimicrobials for systemic use were 36.02% followed by the drugs for acid related disorders i.e. alimentary tract drugs 26.06% and analgesics & antipyretics 18.00%. The details of the therapeutic drugs are given in table

Antibiotics prescribed in hospitalized patients

The most commonly prescribed antibiotics along with cephalosporins in medicine department in study patients was Metronidazole 17.82% followed by Ciprofloxacin 13.86%

Cephalosporins

Number of cephalosporins prescribed during hospital stay

It was found that 89.01% patients received one cephalosporin and 10.99% patients received two drugs in their hospital stay.

Individual drug therapy during hospital stay

The most widely prescribed Cephalosporin in studied patients was found that Ceftriaxone 48.51% followed by Cefotaxime 13.86%.

Comparison of cephalosporin generations used during hospital stay

Third generation cephalosporins 46.16% was the most commonly prescribed class of cephalosporins in medicine department followed by second generation 23.08% use.

Type of ADR

All the reported adverse drug reactions were found to be Type B in nature.

Table 1: Age distribution of patients studied (n=101)

Age in years	Number of patients	Percentage (%)
<20	07	06.93
21-30	23	22.77
31-40	21	20.79
41-50	18	17.82
51-60	28	27.73
61-70	02	01.98
71-80	01	00.99
81-90	01	00.99
Total	101	100.0

Table 2: Gender distribution of patients (n=101)

Gender	Number of patients	Percentage (%) (n=101)
Male	51	50.50
Female	50	49.50

Table 3: Co- morbidity condition of Patients (n=101)

Co-morbid conditions	No	Percentage (%) (n=101)
No	76	75.25
Yes	25	24.75

Table 4: Type of treatment (n=101)

Treatment	No	Percentage (%) (n=101)
Empirical	75	74.26
Specific	26	25.74

Table 5: Site of Infections

Site of infection	No	Percentage (%) (n=101)
Bone and joint	04	03.96
Skin and soft tissue	13	12.87
Upper respiratory tract infections (URTI)	07	06.93
Gastrointestinal infections (GI)	15	14.85
Urinary tract infections (UTI)	17	16.83
Lower respiratory tract infections (LRTI)	13	12.87
Pneumonia	06	05.94
Fever	02	01.98
Otitis media	01	00.99
Sepsis	03	02.97
Central nervous system (CNS)	02	01.98
Brain & meningitis	02	01.98
Sexual transmitted diseases (STD)	03	02.97
Pelvic inflammatory disease (PID)	02	01.98
Ear nose throat (ENT)	02	01.98
Blood	09	08.91

Table 6: Therapeutic class of medication used during hospital stay

Therapeutic class	Percentage (%) (n=101)
Antimicrobial drugs	36.02
Alimentary tract drugs	26.06
Analgesics and Antipyretics	18.00
Respiratory system drugs	10.17
Central nervous system drugs	01.22
Cardio vascular	04.14
Hormonal preparations	01.02
Blood forming agents	04.24

Table 7: Comparison of Antibiotics use along with cephalosporins

Antibiotics co-prescribed	Number of patients	Percentage (%) (n=101)
Amoxicillin+Clavulanic acid	09	08.91
Amoxicillin	05	04.95
Ampicillin	06	05.94
Amikacin	05	04.95
Azithromycine	07	06.93
Ciprofloxacin	14	13.86
Clarithromycin	03	00.02
Clindamycine	02	01.98
Doxycycline	13	12.87
Erythromycine	04	03.96
Gentamicin	05	04.95
Levofloxacin	05	04.95
Metronidazole	18	17.82
Piperacillin+Tazobactam	03	02.97
Penicillin	02	01.98

Table 8: Number of cephalosporins prescribed during hospital stay

No of Cephalosporins	No of Patients (%) (n=101)
One	89.10
Two	10.99

Table 9: Individual drug therapy

Drug Therapy	Total (n=101)	
	No	Percentage (%)
Ceftriaxone	49	48.51
Cefixime	08	07.92
Ceftazidime	07	06.93
Cefotaxime	14	13.86
Cefoperazone	03	02.97
Cefuroxim	04	03.96
Cephalexin	06	05.94
Cefpodoxime proxetil	01	00.99
Cefazolin	03	02.97
Cefaclor	02	01.98
Cefepime	01	00.99
Cefpirome	01	00.99
Cefdinir	02	01.98

Table 10: No of formulations of cephalosporins used during hospital stay

No of formulations	No of patients (%) (n=101)
One	91.10
Two	09.90

DISCUSSION

This study provides the data on the nature and extent of usage of cephalosporins in patients admitted to medicine wards at AH&RC Hospital. A total of 101 Cephalosporins prescribed patients are identified in the medicine ward are included in this study.

Patient characteristics

In our study male population was more (50.50%) than the female (49.50%). This findings is similar to a study conducted by Shankar et al that showed a male predominance (61.6%) compared to females (38.8%).⁵¹ A study conducted in surgery departments at a tertiary care center also showed that a greater proportion of study population was males (52%) than females (48%).¹³

Majority of patients in our study belonged to age group of 51-60 followed by the 21-30 years. And the average ages of male and female patients were 41.98% and 40.02% respectively.

The average length of hospital stay of study patients was found to be 7 days ranging from 3 to 25 days. This was similar to the study conducted in a teaching hospital in Nepal where the median length of stay was 9 days.¹³ In our study it was found that majority of the patients stayed 3-10 days in the hospital which was determined by the severity and co morbidity of patients condition.

In our study about 24.88% of patients have co morbidity conditions. The common co morbid condition observed were hypertension and diabetes followed by respiratory system disorders like COPD and asthma. The use of multiple drugs in our study patients was due to increased number of patients with co-morbid conditions as 24.88% of the study population presented with at least one co morbid condition.

It was observed that 74.26% of patients received cephalosporins for empirical therapy whereas 25.74% received it for specific treatment. In our study it was observed that cephalosporins were prescribed empirically, especially third generation drugs used in higher patients than the other generations. There is no evidence that newer antimicrobials are more effective than older options. The prophylactic use of newer, broad spectrum drugs that are frontline therapeutic agents is generally discouraged because of concern that widespread use will promote the emergence and spread of bacterial strains that are resistant to them.

Majority of hospitalized patients in the medicine ward had UTI (16.83%), followed by GI (14.85%), LRTI (12.87%), Skin & Soft tissue (12.87%), URTI (6.93%), and Pneumonia (5.94%) disorders as the primary disease conditions.

Among the drugs received by the study patients, anti infective drugs (36.02%) were the most commonly received class of drugs, followed by alimentary tract drugs (26.06%), analgesics and antipyretics (18%), respiratory system drugs (10.17%) and central nervous system drugs (1.22%) cardiovascular (4.14%). This findings was similar to the results of a study conducted by Karin et al wherein the most utilized group were drugs for blood and blood forming organs followed by anti infective for systemic use, drugs for alimentary tract and metabolism and central nervous system drugs.⁵⁴ It is obvious that the increased use of anti infective agents and alimentary tract drugs were due to the reason that most of the study patients presented with infectious diseases and digestive system disorders.

Increased use of antimicrobials could be due to their increased use in empirical treatment of infections as well as for surgical prophylaxis. Greater utility of drugs for acid related disorders is not only due to their use in the treatment of gastric disorders, but also due to their use as a prophylactic treatment for potential gastrointestinal disturbance owing to medication use.

The most commonly co prescribed antibiotics in medicine department was found to be nitroimidazoles (17.82%), quinolones (13.86%), followed by macrolides, aminoglycosides, β -lactam antibiotics. Results of our study conducted by MR Ain et al was also found to be comparable to our study where the most frequently prescribed antibiotics were β -lactams and quinolones.¹⁴ Our results are comparable to the results observed in a study conducted by MV Srishyla et al where the most frequently prescribed antibiotics were gentamicine, metronidazole and ciprofloxacin.¹⁵

Ceohalosporins

From our study it was found that majority of admitted patients received cephalosporins accounting to one third of total admission. This wide usage may be due to their broad spectrum of activity, good safety profile and a strong record of efficacy in clinical trials. 89.1% of patients were prescribed with one cephalosporin and in 10.9% of patients two cephalosporins were prescribed during their hospital stay in medicine ward. This finding shows the majority of patients were prescribed with one cephalosporin than two cephalosporins.

In our study it was observed that ceftriaxone 48.51% is most frequently prescribed drug among all the other cephalosporins. This is due to low incidence of ADR and excellent penetration to the body tissues and wide coverage to all bacteria's.

In our study it was found that majority of patients were prescribed with one formulation of cephalosporin 90.10%, where as 9.90% of patients were prescribed with two formulations of cephalosporins in medicine ward respectively.

Majority of hospitalized patients received injection form of cephalosporins 81.18% and oral form is accounted for 18.82%. This finding indicates that injections were the most frequently used formulation of cephalosporins. This may be due to the reason that parenteral formulation results in faster onset of action. Moreover, oral formulation is not a preferred route in post operative patients presenting with nausea and vomiting. Also third generation cephalosporins like ceftriaxone and cefotaxime are more frequently used in our hospital setting and are available only as injection form.

About 42.85% of patients in the medicine ward were prescribed with third generation cephalosporins while second generation cephalosporins were prescribed only 28.57%, when compared with first and fourth generation 14.29% and 14.29% respectively. This result indicated that third generation cephalosporin was the most common used class of cephalosporin in medicine ward compared to other classes of cephalosporins. This extensive use of third generation cephalosporin may be due its extended spectrum of activity against most of the bacteria causing various infections especially against gram negative bacteria when compared to other class/generation of cephalosporins. A study conducted by Jonathan et al showed a higher usage of third generation of cephalosporins which was similar to our results.¹⁶

Incidence of ADR in the study patients was found to be 8.91%. ADR was observed with third generation cephalosporins than with second generation cephalosporins. It was found that majority of the reported ADRs were found to be probable and type Bin nature. Majority of reported reactions were moderate in their severity. Gastrointestinal system and skin were the organ system affected by ADR and of which GI effects were found to be higher. This is due to the reason that cephalosporins have a higher incidence of >2% in causing GI disorders and < 1 % incidence in causing skin reactions. ADRs commonly seen in the study patients were diarrhoea, purities, vomiting and headache.

Studies have reported that antibiotics accounts for almost 50% of pharmacy budget in the hospitals it is due to their widespread use. Various brands of cephalosporins were used in our study population and cost of cephalosporins (range Rs 10-350Rs). The average direct cost incurred for cephalosporins per patient in medicine ward was found to be Rs 1047 for the average of 7.31 days. The average total cost per each patient was found to be Rs 234.69 and cephalosporins cost per day was found to be Rs 143.35. This results indicating that maximum amount is accounted for the cephalosporins during the hospital stay.

CONCLUSION

Cephalosporins especially third generation were widely used in medicine departments to treat various disease conditions. Urinary tract Infections is the major disease condition followed by Respiratory Tract Infections and Digestive system infections were seen in the admitted patients. Antibiotics usage cost is accounted for 70% of total hospital stay.

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