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Original Research Article

A prospective study of antimicrobial utilization in post-operative care unit of a teaching hospital in South India

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ABSTRACT

Background: Surgical site infections, a common cause of morbidity and mortality in hospitalized patients can be prevented using an antimicrobial agent (AMA) as prophylaxis. Inappropriate use of AMA leads to antimicrobial resistance.

Methods: A prospective study was conducted on 208 patients in Owaisi Hospital and Research Centre (OHRC) for a period of 6 months on post-surgical patients admitted in the postoperative care unit. Included in the study were post-operative patients aged 18 years and above, who were willing to participate in the study. Data related to demography of the patients and the AMAs used in these patients was collected and analysed.

Results: Majority of the patients belonged to the age group 50 to 59 years (32%) followed by 40 to 49 age group (23%). Male patients (54%) were more than females. Common route of administration was intravenous (89%) and the most common dosing frequency was thrice a day (54%). Most AMAs were used in combinations. Metronidazole (62%) was the most commonly prescribed AMA, followed by ceftriaxone (55%).

Conclusions: Cephalosporins were the preferred antimicrobials for surgical prophylaxis of aerobic infections prescribed in 74% of cases, while metronidazole was used as the primary antimicrobial agent to prevent anaerobic infections. AMA utilization needs to be continuously evaluated in post-operative units of the surgery departments in order to promote rational prescribing to decrease morbidity, cost of therapy and to contain the problem of developing AMA resistance in the region.

Keywords: Antimicrobial agents, Surgical site infection, Prophylaxis, Drug utilization

INTRODUCTION

Surgical site infections (SSIs) are the most common infections in patients who have undergone surgery, which has led to an increase in hospital stay, healthcare costs, complications, morbidity and mortality. Accounting for about 17% of the hospital acquired infections, SSIs resulted in an increased usage of antibiotics which lowered the morbidity and mortality related to SSIs. However, this increased antibiotic utilization has been a major driving force for development of antibiotic resistance.¹

According to the centre for disease control and prevention (CDC), there are three types of SSIs which includes superficial incisional SSIs (involving only skin and subcutaneous tissue), deep incisional SSIs (involving underlying soft tissue) and organ or space SSIs. Prophylactic use of antimicrobial agents (AMAs) before, during and after surgery reduces and minimizes the incidence of post-operative surgical site infections and complications.² CDC fosters a rational choice and an appropriate use of AMAs, at the same time shunning the irrational practice of excessive use of AMAs for a longer duration than required.

Between 2000 and 2010, consumption of antibiotic drugs had increased by 36%. Brazil, Russia, India, China, and South Africa accounted for 76% of this increase, with India's usage alone of antibiotics increased by 62% from 2001 to 2010. Indians consumed 12.9 billion antibiotic pills in 2010, up from 8 billion in 2001.³ Globally, the two last-resort classes of antibiotic drugs like carbapenems and polymyxins have also showed an increased utilization by 45% and 13% respectively, during this period. Cephalosporins, broad-spectrum penicillins and fluoroquinolones accounted for 55% increased utilization during this 10 year period.³ According to a survey done by Johns Hopkins School of Medicine, India was found to be the leading consumer of antibiotics, with an increased utilization (103%) from 3.2 defined daily doses (DDDs) in 2000 to 6.5 billion DDDs in 2015 and an increased consumption of 8.2 in 2000 DDS per 1000 inhabitants per day to 13.6 DDS per 1,000 inhabitants per day in 2015 (63% increase).⁴

WHO initiated a "global action plan on antimicrobial resistance", with 5 planned objectives.⁵ The objectives were improving awareness and understanding of antimicrobial resistance; strengthening surveillance and research; reducing the incidence of infection; optimizing the use of antimicrobial medicines; ensuring justifiable investment in countering antimicrobial resistance.

Irrational prescriptions are of common occurrence in clinical practice, important reasons of which being lack of knowledge about the rationality of the drug to be used, and also the unethical drug promotion.⁶

This non-judicious, indiscriminate and inappropriate use of AMAs has led to an increased risk of bacterial drug resistance, thereby increasing hospital expenses.^{7,8}

Antimicrobial resistance patterns can vary regionally and even among different hospitals within the same community.

Drug utilisation Study (DUS) was defined by WHO as "the studies of marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences".⁹ DUS are pre requisite for the formulation of drug policies and offer useful methods for teaching and training in drug therapy. DUS identifies the problems that arise from drug usage in healthcare delivery system and highlights the current approaches to the rational use of drugs.¹⁰ AMA Utilization study is synonymous to DUS, in which auditing of AMAs can be done, that enables monitoring and evaluation of AMA prescribing patterns and suggest necessary modifications in prescribing practices to achieve rational therapeutic practice.

The objectives of the present study are to evaluate and compare the utilisation patterns of AMAs in the post operative ward and to generate data on the extent of rationality in prescribing these AMAs.

METHODS

A prospective, observational study was done in Owaisi hospital and research centre (OHRC) for a period of 6 months from November 2018 to April 2019 on post-surgical patients admitted in the postoperative care unit. Approval of the institutional ethics committee was taken before the start of study. A total of 208 patients who met the inclusion criteria, were included in the study, and their data was recorded. Patient profile forms were filled which consisted of details of demography, history, diagnosis and antimicrobial therapy administered to the patients. Information like the generic name of AMA and its combination with other AMAs, their frequency and dosages were collected. National treatment guidelines for antimicrobial use in infectious diseases of 2016 were taken into consideration for evaluation of the data of antibiotic utilization.

Inclusion criteria

Inclusion criteria were patients of age above 18 years of either gender, who has undergone surgery and patients willing to participate in the study.

Exclusion criteria

Patients undergoing minor surgical procedures (where prophylactic AMAs not required), patients with known hypersensitivity to antibiotics, patients with pre-existing infections; patients with liver disease and renal impairment; diabetes mellitus patients; immune-compromised patients were excluded.

Source of data

The data for the study was collected by using medical records like patient case sheets of the in-patients; laboratory investigational data reports.

Method of data collection

Patients were enrolled into the study, after taking their consent by considering inclusion and exclusion criteria. The patient's medical records were reviewed from surgery unit cases and the collected data was entered in the case record forms. The data to be entered comprised of the patient's demographic details like age, sex and disease information including diagnosis. The details of the AMAs prescribed and any other therapy given to the patients were collected in terms of dose, duration, frequency and route of administration. Patients were followed up to the time of discharge and their length of stay in the hospital stay was recorded. Data was collected as per proforma, prepared in advance using WHO criteria, taking into consideration the patient's demographic characteristics, disease condition, AMAs prescribed from the date of admission till discharge as well as the operative notes entered. The surgery status

was assessed for any infection. In case of any surgical site infection, the treatment given for that was also collected.

Data was analyzed according to the WHO/INRUD indicators for number of drugs per prescription, number of antibiotics per prescription, number of drugs prescribed by generic name, number of medicines prescribed from WHO list of essential medicines (EML) and number of injections to be administered per prescription.

Descriptive statistical analysis was done using Microsoft excel software and the results were presented as percentages and means.

RESULTS

A total of 208 patients were included in this study. Age-wise distribution showed that the most number of the patients were seen in the ages ranging from 50 to 59 years, which included 67 patients (32%), followed by those in the 40 to 49 age group with 48 patients (23%). Male patients (54%) were more than females.

Regarding the frequency of drug administration per day, it was found that twice daily regimen was being followed more commonly, as seen in 111 patients (54%).

Most common route of administration was intravenous route (89%). 92% of prescriptions used trade names of AMAs, while only 8% prescriptions used generic names for prescribing AMAs. Most of the AMAs were used in combinations. Cephalosporins were the most preferred group of antibiotics which were prescribed for 74% of patients. The cephalosporins used were ceftriaxone (55%), cefotaxime (14%) and cefoperazone (5%). Metronidazole (62%) was the most commonly prescribed AMA, followed by ceftriaxone (55%).

Table 1: Age distribution of patients.

Age (in years)	Patients	Percentage (%)
<20	6	3
20-29	25	12
30-39	35	17
40-49	48	23
50-59	67	32
60-69	27	13

Table 2: Gender distribution of patients.

Gender	Patients	Percentage (%)
Male	112	54
Female	96	46

Table 3: Frequency of antimicrobial used per day.

	Frequency	Percentage (%)
Once daily	38	18
Twice daily	111	54
Thrice daily	59	28

Table 4: Route through which antimicrobial administered.

Route	Frequency	Percentage (%)
IV	185	89
Oral	23	11

Table 5: Antimicrobial prescribed by generic or trade name.

	Frequency	Percentage (%)
Generic name	191	92
Trade name	17	8

Table 6: Prescribing pattern of antimicrobial agents.

AMAs used	Prescriptions	%
Ceftriaxone and metronidazole	59	28
Cefotaxime and metronidazole	23	11
Ceftriaxone and amikacin	18	9
Ceftriaxone	16	8
Ciprofloxacin and metronidazole	16	8
Ceftriaxone and sulbactam	13	6
Amoxicillin and clavulanic acid	12	6
Amoxicillin, gentamycin and metronidazole	11	5
Cefoperazone and sulbactam	10	5
Ceftriaxone and gentamycin	8	4
Levofloxacin and metronidazole	8	4
Cefotaxime, metronidazole and amikacin	6	3
Piperacillin, tazobactam and metronidazole	6	3
Amoxicillin and gentamycin	2	1

DISCUSSION

In this study, all patients who underwent surgery were administered AMAs as prophylaxis. Most of the patients (89%) received the AMAs via parenteral route, with intravenous route being the one preferred. A similar study done by Khade et al showed that the most preferred route of drug administration was intravenous route in 68% cases.¹¹

In the present study, it was observed that most of the AMAs were used as combinations. Monotherapy of

AMAs was seen in only 16 prescriptions (8%) with the third-generation cephalosporin, ceftriaxone. Also, the most commonly prescribed AMA was metronidazole, which was repeated in 129 prescriptions (62%), followed by ceftriaxone in 114 patients (55%). This finding is contrary to other studies by Sharma et al and Alemkere which showed that ceftriaxone was the most commonly prescribed AMA at 78% and 84% respectively.^{12,13}

Aminoglycoside AMAs, like Amikacin and gentamicin, which covers only gram negative organisms, were prescribed in 24 (12%) patients and 21 (10%) patients respectively. Fluoroquinolones like Ciprofloxacin and levofloxacin were used in 16 (8%) and 8 (4%) patients respectively. Even though fluoroquinolones are proved to be highly effective agents for use in post-operative prophylaxis, they were found to be used less frequently in this study. An increased use of fluoroquinolones will prove beneficial, as it could replace the use of cephalosporins to some extent, thereby alleviating the likelihood of resistance development among cephalosporins.

In this study it was found that a wide range of AMAs were used, covering a broad range of microbial spectrum. Among the combination of AMAs, the most common was ceftriaxone with metronidazole in 59 patients (28%). Kulkarni et al showed that Ceftriaxone along with metronidazole was the most preferred AMA combination (84%) in a similar study.¹⁴ Another study done by Naik et al in India showed similar results as that of our study that metronidazole was the most commonly used AMA.¹⁵ However, in contrast to findings of the present study, a study conducted by Venkateshwar in India, showed cephalosporins to be most frequently used.¹⁶ Khan et al showed that third generation cephalosporin like ceftriaxone was the most prescribed AMA used in 92% cases.¹⁷

The second most common AMA combination in this study was cefotaxime and metronidazole in 23 patients (11%). Ceftriaxone was also combined with amikacin in 18 patients (9%). Piperacillin and tazobactam combination were used in 6 prescriptions in this study, which is not recommended for prophylaxis, unless indicated.

92% of the prescriptions used brand names in this study, which is a similar to a finding by Khade et al in a similar study done in south India, in which 80% of drugs were used as trade names.¹¹

Culture sensitivity testing was not done in any of the cases, and it was observed that most of the prescriptions followed an empirical approach. Polypharmacy was observed in some cases, where AMAs were prescribed along with other drugs like Non-steroidal anti-inflammatory drugs, multivitamins and proton pump inhibitors. Polypharmacy must be avoided for prophylaxis, unless indicated. Most of the AMAs (97%)

prescribed were from EML, except for six prescriptions in which AMAs used were not from the EML. 41 (20%) of prescriptions was found to have AMAs in the form of fixed drug combinations. The average number of antibiotics prescribed per patient was calculated to be 2.14.

An excessive prescribing of AMAs in combinations is irrational, especially for prophylactic use. In order to curb the excess and inappropriate use of AMAs, a hospital formulary enlisting the recommended AMAs is required to be prepared and strictly implemented. Measures are needed to be taken by the hospital for procuring and adequately supplying AMAs enlisted in EML and the prescriber must ensure that the AMAs being prescribed are enlisted in EML provided. There is a need to create awareness among prescribers regarding the current difficult situation of increasing AMA resistance. For this, continuing medical education, workshops and awareness campaigns should be conducted at regular intervals. AMA culture sensitivity testing must be encouraged, to improve therapeutic outcomes, especially in non-responding and complicated SSIs.

Detailed knowledge of rational drug use, antibiotic sensitivity testing and clinical judgment in treating infections is required for the optimal and judicious selection of AMAs. To streamline AMA use in India, antibiotic guidelines need to be implemented in every hospital, which requires more antimicrobial utilization studies to be carried out in our existing setups. There is an urgent need for regular and frequent evaluations of AMA prescription patterns and AMA utilization studies.

CONCLUSION

For surgical prophylaxis of aerobic infections, cephalosporins were the most preferred antimicrobials used in 74% patients. Cephalosporins were used either alone or in combination with other antimicrobials. Among the cephalosporins, ceftriaxone was the most commonly used, followed by cefotaxime. For surgical prophylaxis of anaerobic infections, metronidazole was the most preferred antimicrobial used in 62% patients. Multiple antimicrobials were more frequently used as combinations, which showed an empirical approach while prescribing AMAs. Also, culture sensitivity testing was not done for any of the cases. This inappropriate antimicrobial use had resulted in an increased antimicrobial resistance and higher cost of therapy. Effective use of a hospital formulary, essential medical list and strategies to increase awareness among healthcare professionals about AMA resistance, through continuing medical education and awareness campaigns are the need of the hour. A limitation of the present study is the relatively small number of patients covered, the findings of which do not represent the antimicrobial utilization pattern of the entire population in south India. Further similar studies are required to be done at multiple hospitals and at frequent intervals in south India to give a

better and generalized understanding of the current trends in antimicrobial use and in the process, to curb the development of its resistance in the long term.

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