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Original Research Article

Drug utilization pattern of antimicrobial agents in postoperative patients of major surgery in the general surgical wards at a tertiary care teaching hospital

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ABSTRACT

Background: Antimicrobial agents are prescribed very often inappropriately and have become one of the highly abused drugs. The widespread and indiscriminate use of antimicrobial agents results in emergence of antibiotic resistance. The World Health Organization (WHO) has prioritized the rational use of medications. To evaluate utilization pattern of Antimicrobial Agents in postoperative patients of major surgery.
Methods: This was a non-interventional, observational, cross-sectional study, carried out in General Surgery Department at a tertiary care teaching hospital. Total 385 prescriptions of post-operative cases of major surgeries were analysed, to assess the pattern of antimicrobial agents prescribed, using hospital antimicrobial policy.
Results: In this study number of male patients were 68% and female patients were 32%. Frequency of antimicrobial agents use in 385 patients was 1176 and among them, commonly prescribed antibiotics were metronidazole (92.98%) followed by ceftriaxone (49.35%) amikacin (46.75%) and piperacillin-Tazobactam (36.10%). In 49.35% of patients more than 3 antimicrobial agents were prescribed. Average number of antimicrobial agents per prescription were 3. Effectiveness of antimicrobial agents was confirmed by culture sensitivity report. Culture sensitivity test was done in 326 (84.67%). The percentage of antimicrobial agents used from the hospital antimicrobial policy was 74.82%.
Conclusions: Due to fear of SSI and Hospital acquired infections, use of antibiotics for prolonged postoperative period adds economic burden and development of resistance. Thus, prescribers should be trained for proper implementation of antimicrobial policy and prevention of antimicrobial resistance.

Keywords: Anti-microbials agents, Drug utilization pattern, General surgical wards, Major post operative surgeries

INTRODUCTION

Administration of suitable antimicrobial therapy is indispensable to avoid infection-related morbidity and mortality.[1] Un-warranted antimicrobial use leads to the emergence of multi drug resistant organisms which in turn increases morbidity, mortality and health care cost. The crucial phase in treatment of a disease is appropriate diagnosis, which is based on diagnostic tests and physician's clinical experience. The second crucial phase in treatment is rational prescribing, which itself is based on physician's knowledge on pathophysiology of disease to be treated. Third most crucial phase is appropriate use of drugs by patients and the adherence to instructions given by prescriber. These three phases only lead to the rational drug use.[2]

Studies of prescribing patterns and drug utilization are useful to identify the problems and to provide feedback to prescribers so that we can create awareness about rational use of drugs. Unnecessarily prescribed branded drugs, along with the cost issue and inadequate drugs supply, lack

of patient counselling about the dosing schedules and possible side effects are the major causes of irrational use of drugs, which can lead to therapeutic failure and undesirable side effects.[3]

Antimicrobials are currently the most widely used category of drugs. The prescription of antimicrobials is largely based on the needs of individual patient, type of surgical procedure patient is subjected to, clinical condition and the causative micro-organisms.[4] During the postoperative period the prevalence of infection is high and hence antimicrobials are frequently used empirically. The overwhelming majority of surgical procedures require effectively limited delivery of antibiotic prophylaxis so as to prevent infections. Ineffective antibiotic prophylaxis can lead to the development of surgical site infections (SSIs), which represent a significant global burden of disease.[5]

The widespread and indiscriminate use of antimicrobial agents inevitably has resulted in the emergence of antibiotic resistant pathogens.[6] The World Health Organization (WHO) has prioritized the rational use of medications, hence we aim to evaluate the same, as this data will play an important role in formulating practical guidelines for their rational use.

METHODS

This was a non-interventional, observational, cross-sectional study and was carried out in General Surgery Department at a tertiary care teaching hospital. The study population included the patients in general surgical wards at a tertiary care teaching hospital. This study was initiated after obtaining permission from the Institutional Ethics Committee, (IEC). All the data collected was kept strictly confidential and used only for the purpose of this study. The study included males and females above 18 and less than 65 years of age group. Written informed consent was taken before recruitment of patients in the study.

Data collection

Surgical case sheets and drug charts were recorded in a self -designed proforma. The collected data included the following elements, demographic characteristics, current diagnosis.

Medical history if any and Medications prescribed including (name of the drug, route of administration, frequency of administration, therapy (monotherapy/multiple drugs). (The day of visit was considered as duration of treatment received so far).

Inclusion criteria

Patients in the age group of above 18 years and below 65 years who underwent major surgery and admitted for more than 24 hours in the surgery wards were included in the study. Patients with clean- contaminated (type2) and contaminated (type 3) surgeries.

Exclusion criteria

Patients below 18 years of age and above 65 years. Pregnant and lactating women. Minor surgeries and clean (type1), dirty/ infected (type 4) surgeries. Patients receiving in-patient care in cardiothoracic, neurosurgery, paediatric surgery departments. Patients who are discharged against medical advice within 24 hours of their admission. Patients are not willing to be a part of the study.

The data was collected after getting approval from the Institutional Ethics Committee. It was collected over a period of 1 year from the date of approval of study.

The surgery research plan

The post-operative cases of major surgeries in the General Surgery Department of hospital were analyzed.

Sample size

The sample size was determined according to the following formula

$$N = \frac{Z^2 p(1-p)}{d^2}$$

$$N = \frac{3.96^2 \times 0.5(0.5)}{(0.05)^2}$$

Sample size =384.

The following parameters were noted at time of visit, total number of male and female patients. Average age of male and female patients. Distribution according to type of surgical wound (clean contaminated (type2)/ contaminated (type3)). Average number of anti-microbial agents (AMAs) prescribed per patient.

This was calculated as, total no of AMA prescribed to all patients. Average no of AMA/ patient = Total number of patients. Percentage of Antimicrobials prescribed by generic name. Number of patients receiving single and multiple antimicrobials.

Percentage of fixed dose combination and single agents. The percentage of antimicrobial drugs prescribed from hospital antimicrobial policy. The average number of antimicrobial switching done in patients, till day of visit. Adverse drug reaction, if any.

Antimicrobial policy

For the study of appropriateness of antimicrobial agents, hospital antimicrobial policy was considered as standard. The parameter was to assess the prescribed drugs, according to hospital antimicrobial policy.

Culture and sensitivity

For the study of shift of antimicrobial agents, culture and sensitivity reports were taken into consideration.

Statistical analysis

Appropriate descriptive statistical analysis was done and expressed in percentage and average (mean±SD). All responses were tabulated using Microsoft-Excel 2007 Software. Graphical representations were made wherever necessary. Later, data was analyzed by using Microsoft excel or open office Spreadsheet. Categorical variables were summarized in percentages.

RESULTS

This study was conducted in General Surgical wards at tertiary care teaching hospital. Among the admitted patients a total of 385 patients who fulfilled the inclusion criteria were enrolled in the study. Case record sheets of the enrolled patients were studied.

Data of prescriptions of these patients was collected and analysed. The present study showed 262 (68%) male patients and 123 (32%) female patients. The mean age of male was found to be 44.7 (12.1) and that of females was 43.7 (13.7). The average number of antimicrobials used per patient were 3 (±0.83).

The maximum number of male patients admitted were (68) and were in the age group of 30-39 year. This is followed by (65) male patients in the age group of 40-49 and (62) in the age group 50-59 years, (40) in age group of 60-69 and (23) in age group of 20-29. In this study the female patients admitted were found to be less as compared to males. Maximum number of female patients (29) was from age group of 50-59 (Figure 1). Out of all antimicrobials used, 29.09% were in fixed dose combination preparations (Figure 2).

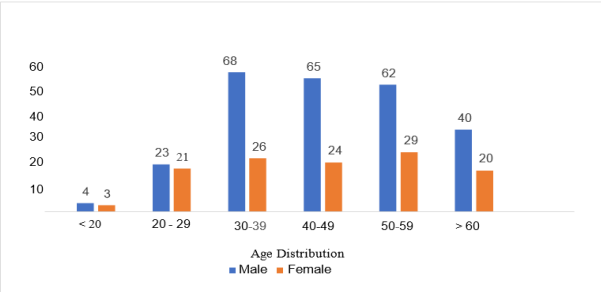


Figure 1: Age wise distribution of study population.

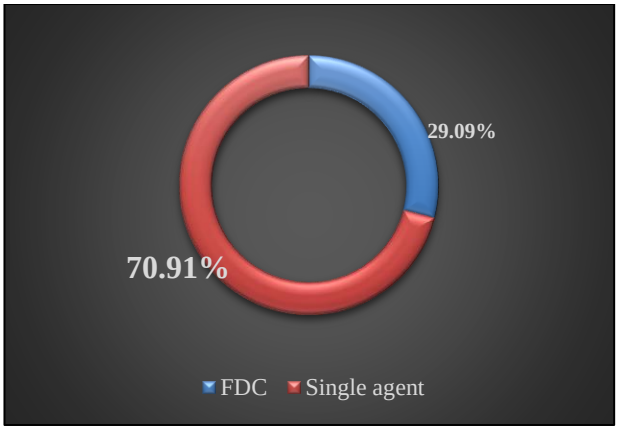


Figure 2: Percentage distribution of FDC and single agents.

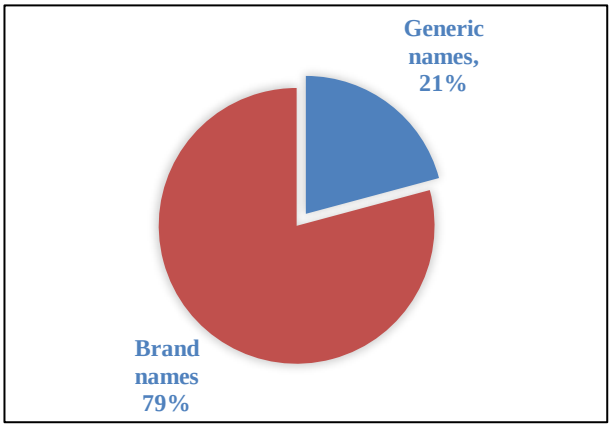
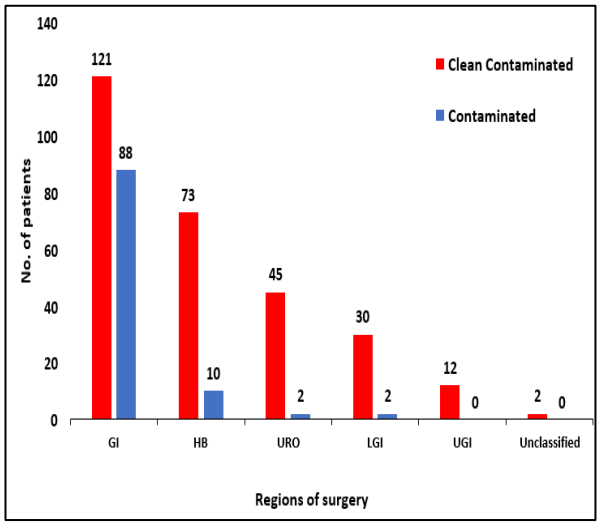


Figure 3: Percentage distribution of generic vs brand name.



UGI=Upper gastrointestinal (Mouth till esophagus), GI=gastrointestinal (stomach to colon), LGI=lower gastrointestinal (rectum to anus), HB=hepatobiliary (including pancreas), URO=urogenital.

Figure 4: Type of surgical wounds in different regions.

The total percentage of drugs prescribed by brand name were 20.49% while by Generic drug 79.51% (Figure 3). The maximum number of patients had acute appendicitis (8.5%), followed by cholecystitis (7%) and then perforated appendicitis (5.2%). Whereas abdomen trauma, prepyloric perforation, fistula in ano and small bowel obstruction were found in same number of patients (4.7%). It was also seen that 209 (54.28%) of patients underwent gastrointestinal surgeries, 83 (21.55%) were of hepatobiliary surgeries. The maximum surgeries performed were of gastrointestinal region (Figure 4). Out of total 385 patients, the culture was positive among 49 patients. In total 39 patients antimicrobial switch was done. The Antimicrobial switch was done according to the culture and sensitivity reports in 27 patients, while in 12 patients switch was done without culture sensitivity report.

The most common organisms found in culture reports included pseudomonas aeruginosa, E. coli, enterococcus and klebsiella. There was a need to specify the type of culture (wound/blood) in the patient's file by the surgeons. Assessment of the pattern of antimicrobial agents prescribed, as per hospital antimicrobial policy: Every patient has received at least one antimicrobial as per the hospital antimicrobial policy. The frequency of antimicrobial administration in this study was 1176, out of which 880 times (74.82%) antimicrobials were used as per the hospital antimicrobial policy.

Table 1: Antimicrobial agents used in the study population.

Antimicrobial agents (AMA)	Number of patients n=385 (%)
Metronidazole	358 (92.98)
Ceftriaxone	190 (49.35)
Amikacin	180 (46.75)
Piperacillin-Tazobactum	139 (36.10)
Ciprofloxacin	80 (20.77)
Amoxycillin-clavulanic acid	62 (16.10)
Gentamicin	51 (13.24)
Cefotaxime	35 (9.09)
Levofloxacin	25 (6.49)
Meropenem	20 (5.19)
Cefoperazone-Salbactum	17 (4.41)
Linezolid	4 (1.038)
Colistin	4 (1.038)
Vancomycin	3 (0.77)
Nitrofurantoin	2 (0.51)
Tigecycline	2 (0.51)
Norfloxacin	2 (0.51)
Ampicillin	1 (0.25)
Cefoxitin	1 (0.25)

Table 2: Distribution among the class of antimicrobial agents.

Class of antimicrobial agent	N (%)
Beta- Lactams	465 (39.54)
Anti-anaerobic/Antiprotozoal	358 (30.44)
Aminoglycosides	231 (19.64)
Fluroquinolones	107 (9.09)
Oxazolidinones	4 (0.34)
Polypeptides	4 (0.34)
Tetracyclines	3 (0.255)
Nitrofuran derivative	2 (0.17)

Table 3: Dosage forms used in study population.

Antimicrobial dosage forms	Frequency of antimicrobial use
Oral dosage forms	30 (2.55%)
Intravenous dosage forms	1146 (97.44%)
Total	1176

Table 4: Distribution of patients as per type of wound.

Type of wound	Number of patients (%)
Clean contaminated (Type 2)	283 (73.51)
Contaminated (Type 3)	102 (26.49)

Table 5: Number of patients receiving monotherapy and multiple antimicrobial agents.

Number of antimicrobial agents	Number of patients	% distribution
1	190	49.35
2	108	28.05
3	69	17.92
4	13	3.38
5	3	0.78
6	1	0.26
7	1	0.26

Table 6: Culture reports among the study population.

C/S samples		Number of patients
Samples sent		326
Samples not sent		59
Culture positive (growth seen)		49
Culture negative (no growth)		277
Antimicrobial switch as per C/S report		27
S. No.	**Antimicrobial switch**	
1	No	336
2	Yes	39
2.A	Antimicrobial switch as per C/S report	27
2.B	Antimicrobial switch without C/S report	12

DISCUSSION

Patient related data

Our study included 385 patients which is a large study of this kind done in a tertiary care hospital in this region. Percentage of male patients was 68% compared to females which was 32%, indicating that a greater number of males were admitted for surgery.

Pattern of drug use

In our study all 385 patients received antimicrobial agents. The frequency of antimicrobial administration in 385 study patients was 1176.

Among them the commonly prescribed antibiotics were metronidazole (92.98%) followed by ceftriaxone (49.35%), amikacin (46.75%), piperacillin-tazobactam (36.10%), ciprofloxacin (20.77%) and amoxicillin-clavulanic acid (16.10%). Least prescribed antimicrobial agents included were ampicillin, cefoxitin 1 (0.25%). Thus, Metronidazole was most used drug in this study. As it is the most effective drug against anaerobic bacteria for prevention of post-operative infections. Other drugs are mainly effective against gram-positive and gram-negative bacteria. Other study like Khade et al, observed that ciprofloxacin (22.7%) and metronidazole (21.56%) were widely used antibiotics.[7]

The study by Salman et al, showed that amikacin was most commonly used.[8] Madkholkar NH et al, also shows metronidazole (72%) as most commonly used antimicrobial drug in their study.[12] In our study amikacin was prescribed in 46.75% of patients. Amikacin has high ototoxic and nephrotoxic potential. Nephrotoxicity is greater in patients with impaired renal function and in those who receive high doses or prolonged therapy. In this study 28.05% patients received 2 antimicrobials while 49.35% patients received 3 antimicrobials and 17.9% patients received 4 antimicrobials. However, in the study by Madkholkar NH et al, 2 antimicrobials were used more commonly. In our study some patients were prescribed with 5 or more antimicrobials, the probable reason may be either due to nonhealing surgical wounds and or non-responsive surgical site infections.

The purpose of antibiotic usage in postoperative patients is prophylactic to prevent post-operative infection at the surgical site. However, the use of antimicrobials in

combination often was irrational and without any evidence. For example, the combined use of Ceftriaxone and Amikacin, despite the known fact that both these drugs have spectrum of action that covers mostly gram- negative organisms. In our study the drugs prescribed by generic name were 79.67%. In other studies, also drugs were prescribed by generic name (87.27%) and (68.24%).[10,11]

However, studies by Bhansali et al 9 (51.43%) and Khade et al, (74.51%) showed higher percentage of drugs prescribed by brand names.[7] It is advisable not to prescribe drugs only for avoiding blanket prophylaxis. This study shows that the fixed dose combination used was 342 (29.09%), this was seen in study by Madkholkar NH et al.[12] All the patients (385) received intravenous antimicrobials. Out of these patients, only 26 patients were shifted to oral antimicrobial therapy. Similar study done by Brethis CS et al and Bhansali NB showed intravenous route of administration as more common.[9,13]

Hospital antimicrobial policy

The hospital antibiotic policy was considered as a standard for comparison and assessment of appropriateness of antimicrobial use. In this study, along with the antimicrobials stated in antimicrobial policy, other antimicrobial agents like amikacin were also prescribed. The use of three antimicrobials was observed in 190 patients (49.35%).

Use of more than five antimicrobial agents was seen in 2 patients (0.52%). Every patient has received at least one antimicrobial as per the hospital antimicrobial policy. The percentage of antimicrobial agents used from the hospital antibiotic policy was 74.82%. The duration of antimicrobial treatment given to the patients in this study was greater than that advised in guidelines of antimicrobial policy.

Culture and sensitivity tests

This study showed that 326 (84.67%) patients underwent antibiotic sensitivity testing. In this study, among the samples only 49 (15.03%) cases showed growth of the organism. Similar study by Madkholkar NH et al, showed change of antimicrobial therapy in 41(12.42%) out of 330 patients after culture and sensitivity report.[12] The most common organisms found in culture reports included pseudomonas aeruginosa, *E. coli*, enterococcus and klebsiella. There is need to specify the type of culture (wound/blood) in the patient's file by the prescribers. Out of total 385 patients, the culture was positive among 49 patients. In total 39 patients antimicrobial switch was done. The Antimicrobial switch was done according to the culture and sensitivity reports in 27 patients, while in 12 patients switch was done without culture sensitivity reports.

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The major limitation of our study was the rate of surgical site infection in different types of surgeries were not evaluated, but the surgeons informed that the rate of SSIs was less. Hence surgical site infections (SSIs) might have been underestimated. This was a cross-sectional study. So, the study did not include the antimicrobials prescribed for the whole duration of hospital stay and at discharge, so actual total duration of antimicrobial use will be more than what is reported in our study.

The culture and sensitivity reports recorded from the patient's files did not mention the site of culture, whether it was wound culture or blood culture reports. Hence, proper specification of the reports is important, so that appropriate shift of antimicrobial agents can be done and monitoring of ADR are essential to reduce harm to patients and thus improve public health. The principal limitation of ADR detection is lack of awareness of what constitutes an ADR. Another reason might be that the post operative patients might not be addressed and the duration of data collection was less, as it was a cross-sectional study.

CONCLUSION

The number of antimicrobials per prescription should be kept minimum to prevent development of resistance and avoid risk of drug interactions. Necessary measures should be taken to enhance prescribing by generic name. Further, surveillance for the implementation of the same is necessary as most of the surgeons prescribe antibiotics as per their personal preference, rather than adhering to specific guidelines.

Due to fear of SSI and Hospital acquired infections, use of antibiotics for prolonged postoperative period adds to economic burden and such use may lead to development of resistance. Thus, prescribers should be trained for proper implementation of antimicrobial policy and prevention of antimicrobial resistance.

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