

Drug Utilization Study on Antimicrobial Agents used in Prophylaxis for Major Surgeries at a Tertiary Care Hospital in Odisha

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Abstract: ***Background and Objective:** This study aims to take a close analytical look at the prescribing patterns of antimicrobial agents used prophylactically for major surgeries at a tertiary care hospital in Odisha. **Method:** a cross-sectional observational study was done; patients above 18 years and receiving antimicrobial therapy pre surgery were included in the study; the medical records of patients who have undergone surgical procedures was verified for antimicrobial prophylaxis with respect to the choice of antimicrobial agent and the time of its administration. **Result:** A total of 103 patients with surgical operations were included in the study. It was found that a total of 307 antimicrobial agents were used in these patients for surgical prophylaxis. Metronidazole was the most prescribed agent followed by Ceftriaxone. Amoxicillin + Clavulanic acid combination was used in 31% cases. The mean number of drugs per prescription was found to be ~ 3 (2.98). **Conclusion:** The rate of prescribing of broad-spectrum antimicrobial agents has increased as they are now routinely employed for prophylaxis of major surgeries. This may lead to the development of bacterial resistance and unnecessary wastage of resources; however, development of guidelines and judicious use of drugs can benefit the patient and reduce the cost of health care.*

Keywords: Drug Utilization Study on Antimicrobial agents used in prophylaxis for major surgeries at a tertiary care hospital in Odisha

1. Introduction

Surgical site infections (SSIs) are a common cause of healthcare-associated infection (1). Surgical site infections (SSIs) are the second most common cause of nosocomial infections (2,3). Patients who develop SSIs are up to 60% more likely to spend time in an intensive care unit, 5 times more likely to be readmitted to the hospital, and 2 times more likely to die than are patients without an SSI (4).

The United States Centre for Disease Control and Prevention (CDC) has developed criteria that define surgical site infection (SSI) as infection related to an operative procedure that occurs at or near the surgical incision (incisional or organ/space) within 30 days of the procedure or within 90 days if prosthetic material is implanted at surgery. These criteria have become the standard and are widely used by surveillance and surgical personnel.

Surgical antimicrobial prophylaxis refers to a very brief course of an antimicrobial agent which is initiated just before surgery, to prevent infections at the surgical site. It is one of the most widely accepted practices in surgery.

Optimal prophylaxis includes an appropriate selection of safe and effective antimicrobials, initial dosing at an appropriate time and redosing if required, in order to maintain effective serum and tissue levels throughout the operation, and discontinuation when the patient is no longer receiving a benefit.

Prophylactic administration of antibiotics can decrease postoperative morbidity, shorten hospitalization, and reduce the overall costs attributable to infections. Principles of prophylaxis include providing effective levels of antibiotics in the decisive interval, and, in most instances, limiting the course to intraoperative coverage only.

Rational choice of antimicrobial agents used for prophylaxis against SSIs is of prime importance to not only reduce the

burden of healthcare associated disease but also to recognize and try to guard against the potential problems that arise from their use.

Clinical judgement is made based on microbiological and pharmacological factors and should aim to provide an optimal and judicious selection of antimicrobial agents used for the various surgical procedures. While increased availability of antibiotics has lowered patient morbidity and mortality it is also one of the major contributors to development of antibiotic resistance.

This study will take an analytical look at the prescribing pattern of various antimicrobial agents used for surgical prophylaxis in major operations to guard against SSI at our hospital.

2. Methods

This is a hospital based cross-sectional observational study conducted on surgical patients for whom surgical procedures were performed and who were given prophylactic antimicrobial agents before surgery at Hi Tech Medical College and Hospital, Bhubaneswar. Patients above 18 years of age of both genders and receiving antimicrobials pre surgery met the inclusion criteria and were included in the study; the medical records of patients who have undergone surgical procedures was verified for antimicrobial prophylaxis with respect to the choice of antimicrobial agent and the time of its administration. A total of 103 patients were included in the study.

Patient details consisting of demography, etiology, history, diagnosis, prophylactic antibiotic use was collected. Evaluation of the data of drug utilization was done using the standard treatment guidelines Scottish Intercollegiate Guidelines Network (SIGN) and the updated combined American Society of Health-System Pharmacists (ASHP) guidelines.

3. Results

A total of 103 patients undergoing surgery and receiving pre op antimicrobial prophylaxis were included in the study. Retrospective analysis of the data collected from the medical records department of our hospital was done for these patients with emphasis on the choice of antimicrobial agents used for prophylaxis in different surgical procedures.

Out of the 103 patients, 66 were male patients and 37 were female (Table 1). 21 patients (20.3%) were in the age group pf 18-32 years; 35 patients (33.9%) were in the age group 33-47 years; 29 patients (28.1%) were in the age group 48-62 years and 18 patients (17.4%) were in the age group 63-77 years (Table 2).

The 103 cases were classified into respective system-wise surgical procedures of which 31 (30%) cases were of skin and soft tissue infections; 33 (32%) were general surgical procedures; 22 (21.3%) were gastrointestinal tract surgical procedures and 17 (16.5%) were surgeries of the hepatobiliary tract (Figure 1).

Out of the 103 patients included in the study 27 (26.2%) had hernia repair; 22 (21.3%) had appendectomy; 17 (16.5%) had cholecystectomy; 7 (6.7%) had diabetic foot ulcer; 19 (18.4%) had abscess (Figure 2).

A total of 307 antimicrobials were used in the 103 patients that were included in the study. The most commonly prescribed antibiotic was Metronidazole (26%) followed by Ceftriaxone (18.8%). Tazobactam (16.9%) in combination with Ceftriaxone or Cefepime or Piperacillin was highly used. The combination of Amoxicillin and Clavulanic acid (20.8%) was used in 31.1% of the total cases. Among other cephalosporins Cefepime (2.6%) was used. The aminoglycoside Amikacin was also used and comprised 10.4% of the total antibiotics given. (Table 3)

The total number of fixed dose combinations was 4; of which (Ceftriaxone + Tazobactam) was used most 37.8 % (39 times) followed by (Amoxicillin + Clavulanic acid) which was used 31.1 % (32 times). (Cefepime + Tazobactam) was used 8 times whereas the combination of (Piperacillin + Tazobactam) was used 5 times.

The study revealed the different antimicrobial agents which were used for prophylaxis of various surgical procedures. In the cases of hernia repair a total of 72 (23.4%) antibiotics were used. Ceftriaxone (6.1%) was prescribed most commonly. Amikacin was also highly used. Tazobactam was combined with Ceftriaxone or Cefepime in a few of these patients. Metronidazole was also used in selected cases.

In the cases of Appendectomy a total of 71 (23.1%) antibiotics were used. Ceftriaxone + Tazobactam combination was used in 77.2 % of these cases while Piperacillin + Tazobactam combination was used in the rest.

Metronidazole was used in all these cases. Amikacin was least used.

In the cases of Cholecystectomy a total of 59 (19.2%) antibiotics were used. Ceftriaxone + Tazobactam combination was used in 70.5% of these cases whereas Amoxicillin + Clavulanic acid combination was used in the rest. Metronidazole was again used in all these cases. Amikacin was used in 47.1% of these cases.

In the cases of Diabetic foot ulcer a total of 21 (6.8%) antibiotics were used. Amoxicillin + Clavulanic acid combination was most commonly used; and was prescribed along with metronidazole to all these patients before surgery.

In the cases of Abscess a total of 57 (18.5%) antibiotics were used. Amoxicillin + Clavulanic acid combination along with Metronidazole was used in all these cases.

In other procedures; Ceftriaxone and Linezolid was used for skin grafting; Ceftriaxone, Linezolid and Metronidazole or Amoxicillin + Clavulanic acid combination was used in cases of Cellulitis; Ceftriaxone, Linezolid and Metronidazole was used for Colostomy procedure.

Among cephalosporins Ceftriaxone was prescribed most times for pre-operative prophylaxis. Metronidazole was the most commonly prescribed antibiotic in this study. Amoxicillin + Clavulanic acid combination and Amikacin were also used in a significant proportion of patients.

Table 1: Demographic details of patients

Sex	Number of patients (%)
Male	66 (64.1)
Female	37 (35.9)

Table 2: Age group categorization

Age	Number of patients (%)
18-32	21 (20.3)
33-47	35 (33.9)
48-62	29 (28.1)
63-77	18 (17.4)

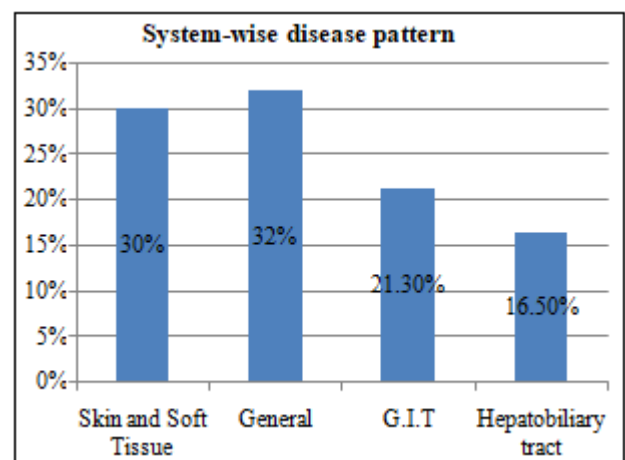


Figure 1

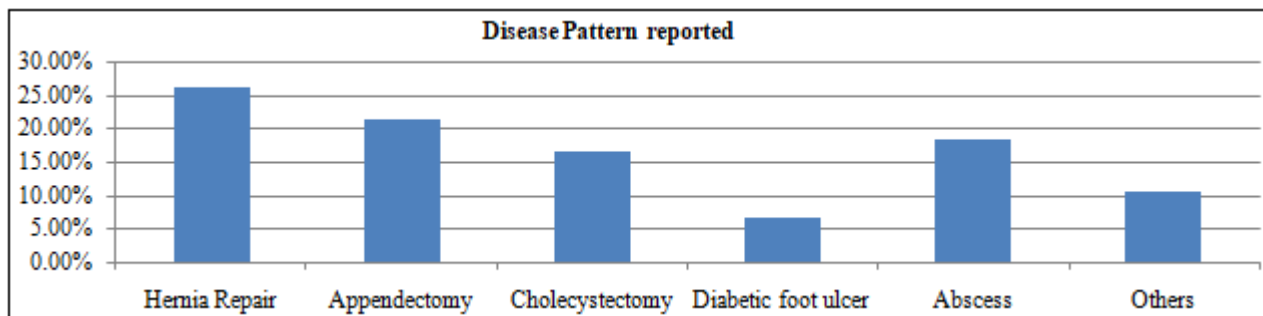


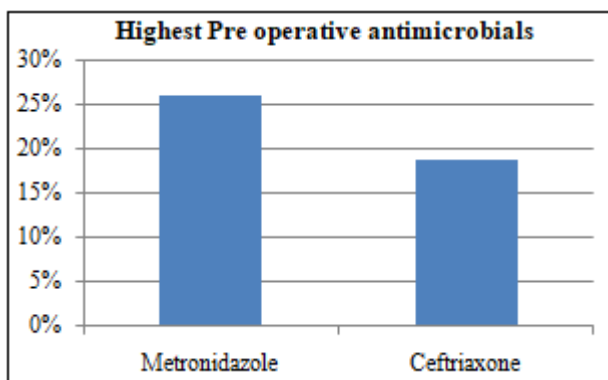
Figure 2

Table 3: Prescribing pattern of pre-operative prophylactic antimicrobials

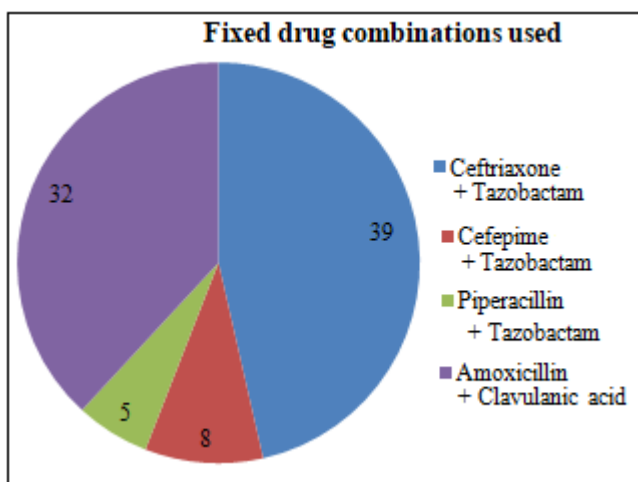
Antimicrobial used	Number of times used	(%)
Metronidazole	80	26%
Ceftriaxone	58	18.8%
Cefepime	8	2.6%
Piperacillin	5	1.6%
Tazobactam	52	16.9%
Amikacin	32	10.4%
Linezolid	8	2.6%
Amoxicillin	32	10.4%
Clavulanic acid	32	10.4%

the elimination of a colonized organism to prevent the development of an infection. This study focusses on primary pre-operative prophylaxis afforded by the use of various antimicrobial agents.

Although antimicrobial prophylaxis plays an important role in reducing the rate of SSIs, other factors such as attention to basic infection-control strategies, the surgeon’s experience and technique, the duration of the procedure, hospital and operating-room environments, instrument sterilization, preoperative preparation (e.g., surgical scrub, skin antisepsis, appropriate hair removal), perioperative management (temperature and glycaemic control), and the underlying medical condition of the patient may have a strong impact on SSI rates (6).



Prophylactic administration of antibiotics inhibits the growth of contaminating bacteria thus reducing the risk of development of surgical site infection. Administration of antibiotics also increases the prevalence of antibiotic-resistant bacteria (5). This is one of the reasons breakthrough infections occur in some cases despite antibiotic cover. Pre-operative antimicrobial prophylaxis is usually given in all surgical procedures not classified as clean; it may also be given for clean procedures when it is associated with risk factors (Table) (7). Choice of antimicrobial agents for prophylaxis is left to the clinical judgement of the surgeon which is based on standard guidelines and knowledge of local microbial prevalence and antibiotic resistance patterns.



According to standard guidelines pre-operative prophylaxis should be given within 1 hour before the procedure. In some cases prophylaxis may be given 2 hours before the procedure. Our hospital’s policy varied slightly from this as pre op antibiotic prophylaxis was given within 4 hours of the start of procedure.

According to SIGN guidelines the goals of prophylactic administration of antimicrobial agents to reduce the risk of SSIs include use of antibiotics in a manner that is supported by evidence of effectiveness, to minimize the effect of antibiotics on the patient’s normal bacterial flora, to minimize adverse effects and interactions and cause minimal change to the patient’s host defence.

4. Discussion

Prophylaxis refers to the prevention of an infection and can be characterized as primary prophylaxis, secondary prophylaxis, or eradication. Primary prophylaxis refers to the prevention of an initial infection (6). Secondary prophylaxis refers to the prevention of recurrence or reactivation of a pre-existing infection. Eradication refers to

In this study of the total 103 patients; 66 (64.1%) were male and 37 (35.9%) were female. From the total number of patients maximum (35; 33.9%) were in the age group 33-47 years while minimum (18; 17.4%) were in the age group 63-77 years. A study conducted on antibiotic utilization pattern at Bharati Vidyapeeth Deemed University, Pune showed

similar gender distribution i.e. male patients are greater than female patients and comparable data in age group distribution.

The 103 cases were classified into respective system-wise surgical procedures of which 31 (30%) cases were of skin and soft tissue infections (diabetic foot ulcers, abscess, cellulitis); 33 (32%) were general surgical procedures (hernia repair, colostomy closure); 22 (21.3%) were gastrointestinal tract surgical procedures (appendectomy) and 17 (16.5%) were surgeries of the hepatobiliary tract (cholecystectomy). A similar study conducted on antibiotic prescribing patterns at Rajah Muthiah Medical College Hospital in Tamil Nadu showed closely related system wise distribution of surgical procedures for which antimicrobial prophylaxis was given.

Of the 103 patients included in the study maximum 27 (26.2%) had hernia repair; 22 (21.3%) had appendectomy; 17 (16.5%) had cholecystectomy; 7 (6.7%) had diabetic foot ulcer; 19 (18.4%) had abscess. A similar Study on the Usage Pattern of Antimicrobial Agents for the Prevention of Surgical Site Infections (SSIs) in a Tertiary Care Teaching Hospital (8) showed that of all the cases studied 40% were of hernia repair, 36 % were cases of appendectomy, 9% thyroidectomy, and cholecystectomy 7% while the remaining 8% were cases of other procedures. Our study showed a lower (but still significant) incidence of hernia repair and appendectomy. A higher incidence of cholecystectomy and abscess was observed compared to the above mentioned study. Most similar studies conducted in India have a significant proportion of appendectomy and hernia repair cases and this was validated in our study with the combination comprising 47.5% of the total cases.

In this study, it was found that 307 antimicrobial agents were used for prophylaxis in a total of 103 patients undergoing surgical procedure. The antibiotic used most times was Metronidazole (26%) followed by the third generation cephalosporin Ceftriaxone (18.8%). Ceftriaxone was often used in fixed combination with Tazobactam (25.4%). Amoxicillin + Clavulanic acid combination (20.8%) was also highly used. The aminoglycoside Amikacin (10.4%) was given prophylactically in a proportion of cases. Cefepime + Tazobactam and Piperacillin + Tazobactam were the other fixed drug combinations that were used. A similar study conducted on antibiotic utilization pattern at Bharati Vidyapeeth Deemed University, Pune showed Ceftriaxone to be the most commonly used antibiotic for prophylaxis followed by Metronidazole and then Amoxicillin + Clavulanic acid combination. Our study results differed slightly from this as Metronidazole was prescribed most times followed by Ceftriaxone and then Amoxicillin + Clavulanic acid combination. In hospitals injectable antibiotics are used more due to morbid condition of the patients (9). Another study conducted on antimicrobial utilization pattern for surgical prophylaxis to prevent SSIs also reported that third generation cephalosporins were most used followed by Metronidazole (13).

Another study conducted in a tertiary care hospital of Pondicherry showed that cephalosporins (35.6%) and

penicillins (21.3%) were the most commonly prescribed antibiotics (10); however this data was collected from the hospital's intensive care unit and reflected general antibiotic use whereas our study focussed on pre-operative prophylaxis given to patients undergoing surgery.

Ceftriaxone (18.8%) and Cefepime (2.6%) were the two drugs from the class of cephalosporins which were used for prophylaxis in this study. Cephalosporins are an important class of drugs which have been used extensively both for prophylaxis of major surgeries and also for the treatment of bacterial infections (11). They have been very successful in treating, controlling and preventing infection. However, there are a growing number of reports of resistance to these agents with increasing use. Cephalosporins' usage pattern exerts a significance influence over the rates of resistance observed and led to problematic multidrug resistant nosocomial pathogens (12).

This study showed that our hospital had an independent policy for surgical prophylaxis which differed from the revised ASHP guidelines. For cases of hernia repair (both hernioplasty and herniorrhaphy) according to above guidelines recommended first line agent for prophylaxis was Cefazolin. In our study of the 27 cases of hernia repair 18 were mesh hernioplasty procedures while 9 were non mesh herniorrhaphy; a total of 72 (23.4%) of the antibiotics were given. For mesh hernioplasty procedures Cefepime + Tazobactam combination with Metronidazole was used in 8 cases while Ceftriaxone + Tazobactam combination with Amikacin was used in the remaining 10 cases. Ceftriaxone with Amikacin was used in the 9 cases of mesh herniorrhaphy. Cephalosporins' [Ceftriaxone (6.1%) and Cefepime (2.6%)] was the most used class of antimicrobials for hernia repair and this was in keeping with standard guidelines. The choice of cephalosporin to be used however varied.

For appendectomy procedures of uncomplicated appendicitis cases standard guidelines recommend the use of either Cefoxitin, Cefotetan, Cefazolin along with Metronidazole. In our study of the 22 cases of appendectomy; 17 were laparoscopic procedures while the remaining 5 were open procedures; a total of 71 (23.1%) of the antibiotics were given. For laparoscopic cases Ceftriaxone + Tazobactam combination was given with Metronidazole whereas in open cases Piperacillin + Tazobactam combination with Metronidazole and Amikacin was given. It was seen that Ceftriaxone + Tazobactam combination (11%) was most given in laparoscopic appendectomy cases whereas Piperacillin + Tazobactam combination (3.2%) was given in open appendectomy cases. Metronidazole was given in all cases of appendectomy (both open and lap). Amikacin (1.6%) was least used.

For cholecystectomy (both open and 'high risk' laparoscopic procedure) standard guidelines suggest the use of either Cefazolin, Ceftriaxone, Cefoxitin, Cefotetan or Ampicillin + Sulbactam combination. Metronidazole is listed as an alternative agent which may be used. In our study of the 17 cases of cholecystectomy 14 were carried out as laparoscopic procedures while the remaining 3 were open procedures; a total of 59 (19.2%) of the antibiotics were

given. Metronidazole (5.5%) was used in all (both open and lap) cases. Ceftriaxone + Tazobactam combination (7.8%) was used in 9 out of the 14 laparoscopic cases and in all the open cases; Amoxicillin + Clavulanic acid combination (3.2%) was used in the remaining 5 laparoscopic cases. Amikacin (2.6%) was another antibiotic used.

For diabetic foot ulcer and abscess standard guidelines suggest the use of flucloxacillin + ciprofloxacin and metronidazole. In this study there were 7 cases of diabetic foot ulcer; a total of 21 (6.8%) antibiotics were given. All diabetic foot ulcer patients were given Amoxicillin + Clavulanic acid combination (4.5%) and Metronidazole (2.3%). For abscess which comprised of 19 cases in the study and for which 57 (18.5%) antibiotics were given similar to diabetic foot ulcer all patients received Amoxicillin + Clavulanic acid combination (12.3%) and Metronidazole (6.1%). Therefore it was seen that for both Diabetic foot ulcer and Abscess cases Amoxicillin + Clavulanic acid combination and Metronidazole were highly prescribed.

The remaining 11 (10.6%) cases included in the study comprised of skin grafting (3) for which Ceftriaxone and Linezolid was used, Cellulitis (2) for which Ceftriaxone, Metronidazole and Linezolid or Amoxicillin + Clavulanic acid combination was used and Colostomy procedure (6) for which Ceftriaxone and Metronidazole or Ceftriaxone, Metronidazole and Linezolid was used.

This study showed that the antibiotic used most frequently for pre-operative prophylaxis was Metronidazole (26%) followed by Ceftriaxone (18.8%). These results were in keeping with other studies conducted on similar topic which also showed high use of Ceftriaxone and Metronidazole for surgical prophylaxis.

In this study the average number of drugs per prescription was 2.98. This was similar to what was seen in similar studies where the average number of drugs per prescription hovered around 3. Most of these studies such as the one conducted on antibiotic use in Bharati Vidyapeeth Deemed University, Pune and the one conducted in SRTR Government Medical College, Maharashtra focussed on both prophylactic and general use of antibiotics in the surgery department while our study focussed only on antibiotics given for pre-operative prophylaxis.

From the results of this study and after a review of relevant literature it was established that appropriate rational antimicrobial prophylaxis can reduce the risk of Surgical Site Infections (SSIs) and prove beneficial to the patient. However it is also true that widespread use of broad spectrum prophylactic antibiotic cover enhances the selection pressure and leads to the development of antimicrobial resistance.

5. Conclusion

This study showed that the hospital policy for antimicrobial prescribing for surgical prophylaxis of different procedures was slightly different to what is suggested in standard guidelines. Metronidazole was the most prescribed

antimicrobial agent followed by Ceftriaxone. Both Ceftriaxone + Tazobactam and Amoxicillin + Clavulanic acid fixed drug combinations were highly used. The average number of drugs per prescription was roughly 3 (2.98).

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