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Antimicrobial Prophylaxis in Fracture Fixation and Trauma Surgery Patients in Orthopaedics Department of a Tertiary Care Hospital

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ABSTRACT

Background Appropriate use of antimicrobial prophylaxis in orthopedic fracture fixation and trauma surgeries reduces the risk of surgical site infection, however, there do not exit suitable information regarding the timings, duration, and choice of prophylactic antibiotics to be used in orthopedic fracture fixation and trauma surgery. The present study aims to give the brief idea about the appropriate use of antimicrobials and highlight their role as prophylactic agents in preventing the surgical site infections in orthopedic fracture and trauma cases. **Methodology** This prospective, cross-sectional (observational study) collected the demographic, diagnostic and therapeutic data from 100 bone fracture and trauma patients. The study was carried out for six months in Orthopedics Department of a Tertiary Care Hospital in Hyderabad, Telangana, India. **Results** In this study among 100 bone fracture and trauma patients physician preferred second-generation cephalosporin (Cefuroxime) given preoperative in 54% and fourth generation cephalosporin (Cefepime) given postoperative in 64% as the first-line infection prophylaxis. The first Surgical Antimicrobial Prophylactic (SAP) dosage was administered at the time of induction of anesthesia for all the 100 patients. Further 39% patients were treated with single SAP dose, 45% were treated with two SAP doses and 16% were treated with multiple SAP doses. Duration of prophylaxis was confined to 1-day preoperative SAP dose and at least 3- days' postoperative SAP dose, however, the postoperative duration of prophylaxis was increased in few patients according to their wound infection. The physician followed the overall treatment regimen according to the SAP guidelines and this manifested to prevent and control the risk of surgical site infection among all the patients with 1-2 patients suffering from mild ADRs. **Conclusion** This study showed that the prevention of risk of surgical site infection was achieved in all the bone fracture and trauma patients. We assume that this study provides local clinical data as to which regimen may be used in a particular patient. However, National Level Clinical Trials are required to further ascertain this conclusion.

INTRODUCTION

Surgical site infections occur about 30 days after surgery or about one year in patients receiving implants and affect either the incision or deep tissues at the surgical site[(1)].Infection in orthopedic surgery is one of the most dreaded complications. The most common microbes found at the orthopedic surgical site infections are as follows Staphylococcus species including Methicillin-Resistant *Staphylococcus aureus* (MRSA), Acinetobacter, Pseudomonas species and Enterococcus species [(2)].Bone fractures and post-traumatic orthopedic conditions are diagnosed with a combination of a physical examination and imaging. Fractures are diagnosed using X-rays. Depending upon the severity and location of the break or post-traumatic injury – as well as the extent of damage to surrounding tissue, arthograms (X-rays of the joints), computed tomography (CT), and magnetic resonance imaging (MRI).[(3)] SAP guidelines generally recommended a single standard intravenous therapeutic dose of antibiotic in the majority of procedures.[(4-7)] Repeated doses were only indicated in special circumstances like prolonged surgery with a duration longer than the half-life of the antibiotic used or in major blood loss.

The efficacy of SAP relies on the timing of the drug administered so that bactericidal concentrations are established in serum and tissues when an incision is made, and therapeutic concentrations in serum and tissue are maintained throughout the operation until at most a few hours after wound closure in the operating theatre[(8)].Generally, the SAP guidelines recommended that the time of antimicrobial administration should be within 30–60 minutes before the skin incision[(4,5)].Antibiotic resistance pattern may differ among countries. Indian data on timings, duration, and choice of antimicrobial prophylaxis in fracture fixation and trauma cases are scarce. Thus the present study aimed at giving the brief idea and highlight the role of suitable antimicrobials as prophylactic agents in preventing SSI in bone fracture and trauma patients.The standard first-line therapies used were Cefuroxime (750mg) b.i.d (twice daily) given pre-operative and Cefepime (1 g) b.i.d (twice daily) given post-operative. Cefotaxime (500 mg) b.i.d , Teicoplanin (400 mg) b.i.d and Linezolid (600 mg) b.i.d were the other choice of agents given post-operative. The patients were administered single and multiple SAP doses depending upon their wound severity, however, Local data must be considered before commencing on use of multiple SAP doses owing to the development of antibiotic resistance.

METHODOLOGY

The study is a prospective, cross-sectional observational study administering suitable prophylactic antibiotic regimen daily in fracture fixation and trauma patients of Orthopedics department of a Tertiary Care Hospital in Hyderabad. Patients were recruited by consecutive sampling method. Bone fracture and trauma patients were confirmed through physical examination and X-ray diagnosis, patients of all age groups and both the genders were included in the study. Patients who had been on therapeutic antibiotics before surgery, who needed further surgery within 72 hrs., information about the intraoperative use of antibiotics was lacking, surgery for infants, cancer, gynecological purposes as well as surgery that did not imply clear regimen for prophylaxis and SAP guidelines were excluded from the study. The study was carried out for six months from December 2016 to May 2017. The Institutional Ethics committee of Owaisi Hospital and Research Centre approved the study.

Data collection

We collected demographic, clinical and therapeutic data from bone fracture and trauma patients. The study required a minimum of two visits during the six months survey. Patients were recruited by the consecutive sampling method. We included only those cases where we are able to get all data from beginning to end of therapy. The data were collected from the patient's treatment charts/case sheets, laboratory reports, medication bills and patient's attendees. All subjects gave informed consent to participate in the study and allowed the use of-of their personal data for research purposes. First physical examination X-ray tests were performed at the beginning of the study for detection of the type of fracture and trauma. Then tissue samples from the wound site were drawn for the microbiological culture test, other tests like CBP, urine analysis, electrolytes, biochemistry, LFT were performed.

Statistical analysis

Descriptive statistics were used to analyze the demographic, clinical and treatment characteristics of the study population.Outcome variables were represented as percentages.

RESULTS

In this observational study, the efficacy of the different antibiotics was evaluated and determined in hundred patients. Among hundred patients 65%, patients were males and 35%

patients were females. The most common age group among males was between 31 and 49 years and among females was between 50 and 69 years [Table 1], uneducated with the monthly income of less than Rs 10,000. In general majority of fractures in males were as a result of accidents and among females were as a result of age-related bone loss due to menopause and osteoporosis [Table 4].The common comorbidities observed in surgical patients were hypertension in 19% patients, diabetes mellitus in 12% patients, Coronary artery disease was seen in 2% of them and 1% of them suffered from osteoarthritis [Table 5].

Table 1: Age and Gender Distribution:

AGE GROUPS	MALE	FEMALE	TOTAL	PERCENTAGE
<18	14	5	19	19%
18-30	17	3	20	20%
31-49	27	6	30	33%
50-69	10	11	21	21%
>69	0	10	10	10%

Table 2 : Comorbid conditions seen in surgical Patients :

COMORBID CONDITIONS	NUMBER	PERCENTAGE
Hypertension	19	19%
Diabetes Mellitus	12	12%
Coronary artery disease	2	2%
Osteoarthritis	1	1%

Table 3: Fractures seen because of increasing age and bone loss among the surgical patients in the study:

AGE	CAUSE OF FRACTURE	MALES	FEMALES
<18-30	Accidents	31	8
31-49	Bone loss in females +Accidents	24	6
50-69	Menopause +Osteoporosis	10	11
>69	Osteoporosis + Menopause	0	10

Table 4: Types of fractures observed in the study

DIAGNOSIS(TYPE OF FRACTURE)	MALES	FEMALES	TOTAL	PERCENTAGE (%)
# Both bones of leg	4	4	8	8%
# of metatarsals and phalanges	5	0	5	5%
# Distal Radius	10	1	11	11%
# of Humerus	6	5	11	11%
# of Femur	8	7	15	15%
# of Tibia and Fibula	13	4	17	17%
# of Calcaneum	2	0	2	2%
MM tear	8	2	10	10%
# of facial bones	2	0	2	2%
# of ulna	1	0	1	1%

Table 5: Types of trauma cases observed in the study

DIAGNOSIS(TRAUMA)	MALES	FEMALES	TOTAL	PERCENTAGE
Cellulitis of left leg	1	0	1	1%
Post-op case of polytrauma	1	0	1	1%
Non healing ulcer of left foot	1	0	1	1%
Skin grafting of left foot	1	1	2	2%
Tendon rupture of hand fingers	1	0	1	1%
Laceration and loss of skin	1	0	1	1%
Crush injury	0	2	2	2%
Soft tissue injury	1	1	1	1%
Raw area over right leg (knee amputation)	0	1	1	1%
Incision and drainage	2	0	2	2%

Major presenting complaints were pain and swelling at the site of injury. The common diagnosis among bone fracture and trauma patients was by physical examination and X-ray diagnosis, which displayed the type and site of bone fracture in the patients. Even

microscopic culture test was performed to get an idea whether any microbes are residing at wound or site of injury. As the adverse effects associated with antibiotic regimens were minor, they were managed easily.

Efficacy analysis of prophylactic agents

The various prophylactic agents used were Cefepime 1g, Cefuroxime 750 mg, Cefotaxime 500 mg, Teicoplanin 400 mg, Linezolid 600 mg. Physician preferred second-generation cephalosporin Cefuroxime 750 mg given preoperative and fourth generation cephalosporin Cefepime 1 g given postoperatively as a first- line infection prophylaxis. The first SAP dosage was administered at the time of induction of anesthesia in all 100 patients [Table 7]. The number of SAP doses per surgical procedure differed depending upon the patients need 39% patients were given single SAP dose, 45% patients were given two SAP doses and 16% patients received multiple SAP doses [Table 8]. Two cases of mild ADRs were observed among patients treated with prophylactic agents the two patients being treated with Teicoplanin 400 mg and Cefepime 1 g developed rashes and itching sensation all over the body, which was then eradicated after treating with Pheniramine maleate 25 mg [Table 10]. Duration of prophylaxis varied among patients from 4-5 days to even 10 days after surgery, administration of SAP dosage preoperative and postoperative resulted to be more efficacious. Efficacy was presented as the prevention rates, In our study, the total prophylactic antimicrobial treatment regimen achieved 100% prevention of surgical site infection in bone fracture fixation and trauma surgery.

Table 6: Antimicrobial choice agents commonly used in sap practice and agents used in the study.

ANTIMICROBIAL AGENTS	DRUGS	TOTAL (%)
1st generation cephalosporins	-	0 %
2nd generation cephalosporins	Cefuroxime	54 %
3rd generation cephalosporins	Cefotaxime	12 %
4th generation cephalosporins	Cefepime	66 %
B-lactam resistant penicillins	Tazobactam	0 %
Extended spectrum penicillins	Amoxicillin	1 %
Other Antimicrobials	Amikacin, Teicoplanin, Linezolid, Ceftriaxone	28 %

Table 7: Timing of First SAP dosage:

TIME IN HOURS	TOTAL %
>2 hr before operation /surgery	-
1-2 hr before operation	-
< 2 hr before operation	-
At the time of induction of Anesthesia	100 %
After surgery	-

Table 8: Pre-operative and post-operative administration of sap dosage :

DRUGS	DOSE	PRE-OPERATIVE	POST-OPERATIVE
Cefuroxime	750 mg	54 %	2 %
cefepime	1 gm	8 %	64 %
Cefotaxime	200 mg	7 %	14 %
Amikacin	500 mg	6 %	15 %
Teicoplanin	400 mg	0 %	16 %
Linezolid	600 mg	1 %	1 %

Table 9: Number of SAP doses per surgical patients

DOSES	NO OF PATIENTS (TOTAL (%)
1 dose	39
2 doses	45
>2 doses	16

Table 10: Adverse drug reaction and its management

DRUG	ADR	NO OF PATIENTS	MANAGEMENT
TEICOPLANIN (400mg)	Itching all over the body + rashes	1	Inj AVIL (Pheniramine maleate) 25 mg
PRIME(1 g)	Itching all over the body	1	Inj AVIL (pheniramine maleate) 25 mg
DYNAPAR(75mg)	Acute gastritis – 12-15 episodes of vomitings, postoperative fever	1	SypSucral 15ml BD Inj Pan 40 mg IV TID Inj Metoclopramide 10 mg IV TID

Naranjo's causality assessment scale for above three patients:

Questions	Yes	NO	Don't Know	Score
1-Are there previous conclusive reports on this reaction?	-1			-1
2- Did the adverse event appear after the suspected drug was administered?	+2			+2
3- Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1			+1
4- Did the adverse drug reaction reappear when the drug was readministered?			0	0
5- Are there alternative causes (Other than the drug) that could solely have caused the reaction?		+2		+2
6- Did the reaction reappear when a placebo was given?			0	0
7- Was the drug detected in blood(Or other fluids) in a concentration known to be toxic?			0	0
8- Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?			0	0
9- Did the patient have a similar reaction to the same or similar drugs in any previous exposure?		0		0
10- Was the adverse event confirmed by objective evidence?	+1			+1
TOTAL SCORE				**+5**

Interpretation: Naranjo's causality assessment has shown a score of +5 indicating a "Probable"(5-8) causal association among all the three patients with suspected ADRs.

Table 11: Co-prescribed drugs with antimicrobials:

DRUGS	EXAMPLE	NUMBER	PERCENTAGE
H2 receptor blockers	Ranitidine	71	71%
Proton pump inhibitors	Pantoprazole, Rabeprazole	12 49	12% 49%
Calcium and Vit D3 supplement	Calaros	100	100%
Anti-inflammatory enzymes	Enzomac forte	100	100%
Anti-histamines	Avil	2	2%
Vitamin supplements	Lupifit	100	100%
Enoxaparin sodium	Clexane	8	8%
Aspirin	Ecospirin	3	3%
NSAIDs, **Opioid analgesic**	Diclofenac, Tramadol	86 19	86% 19%

DISCUSSION

SAP drugs include second and fourth generation cephalosporins, cefepime, cefuroxime, cefotaxime, others like linezolid, amikacin, teicoplanin. The efficacy of SAP depends on several factors, including a selection of appropriate antibiotic, the timing of administration, dosage, duration of prophylaxis and route of administration. In many institutions around the globe, evidence-based guidelines have been developed to advance the proper use of SAP[(9)].The introduction of antimicrobial prophylaxis has resulted in the reduction of surgical site infections. Surgical antimicrobial prophylaxis (SAP) refers to a very brief course of antibiotic given just before the surgery. Thus, prophylactic antibiotic does not serve the purpose of preventing surgical site infections caused by postoperative contamination[(10)].The goals of SAP are to reduce surgical site infection rates, using antibiotics based on evidence of effectiveness, minimizing the alteration on the patient's normal bacterial flora, minimizing adverse effects and causing the minimal change to the patient's host defenses [(11)]. Our study revealed that prophylactic antibiotic regimen was more effective with mild ADRs observed in only two patients and multiple therapies was given to only 16% patients among hundred patients because prolonged use of prophylaxis can lead to the emergence of resistant bacteria strain[(12)].

Majority of our study population is uneducated, in the age group of 31 - 49 years and belonging to lower socioeconomic status. To the best of our knowledge currently, there are

no Indian studies focusing predominantly on appropriate prophylactic antibiotic use in bone fracture and trauma surgeries.

The duration of prophylaxis varies among patients; the controversy persists in the administration of antibiotics varying from a single dose to 3 doses to 5 days or 14 days.[14] Musmar *et al*. suggest that antibiotics should be discontinued within 24 h after the end of surgery to prevent the emergence of resistance.[13] Those *et al*.[15] recommended prophylactic antibiotic regimen at the time of induction of anesthesia and two subsequent doses at 8 and 16 h postoperatively. Another study by Andersson *et al*.[17] suggests same recommendations of 3 doses within 24 h. Stefánsdóttir *et al*. recommended two doses, one at the time of induction and another 6 h after surgery.[18] Niimi *et al*.[16] in a retrospective study compared the outcome of 1-day intravenous administration with that of long-term intravenous administration in arthroplasty cases. They used antibiotics for 1-day (n = 233) and for at least 3 days (n = 104). The timing of administration remains once again controversial. It varies in different studies from 15 min to 120 min before the skin incision. Yeap *et al*. advocated administration of antibiotics 30–60 min before the surgery or at the time of induction of anesthesia or at least 10 min before inflation of tourniquet.[14,15,16,17]In our study the first SAP dosage was administered during the time of induction of anaesthesia in all 100 patients, duration of prophylaxis was about one day preoperative and for at least 3 days after surgery, however, duration was increased for up to 4-5 days and even for about 10 days postoperatively depending on type and severity of the injury. Overall effectiveness of prophylactic antibiotic regimen was found to be suitable and achieved 100% prevention of surgical site infection.

There are several limitations to our study. The study sample used was small. Due to time constraints, the study was performed as an observational study containing a smaller number of patients. Hence sample size and power estimation calculations were not done. There was a lack of retrospective data for this study. We did not stratify the sample based on the socioeconomic status, cost-effectiveness, adjusting factors to account for the influence of the comorbidities on bone fracture and trauma injuries. We could not give an account of drug interactions among prophylactic antibiotics and suspected serious ADRs over long-term use of prophylactic agents. We did not have data on pharmacy dispensing and or medication compliance in case of patients after discharge. In such cases, there is a risk of overestimation of drug use.

CONCLUSION

Our study showed that prophylactic antibiotic treatment regimen according to SAP guidelines was effective in preventing surgical site infections in bone fracture fixation and trauma surgeries. We assume that this study provides local clinical data as to which regimen may be useful in a particular patient. National Level Clinical Trials are required to further ascertain this conclusion.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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