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A Study to Compare the Efficacy of Single Doseceftriaxone Pre-Operative with Multiple Dose Ceftriaxoneregimen post-Operatively for Surgical Prophylaxis

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ABSTRACT

Objectives: Surgical site infections (SSI) are one of the most common post-surgical complications in all types of surgeries. Antibiotic prophylaxis is usually employed to prevent SSI. This study was done with an aim to compare the efficacy of single dose pre-operative ceftriaxone versus multiple dose post-operative ceftriaxone for surgical prophylaxis.

Methods: This was a prospective, randomized study carried out in the department of surgery at a tertiary care hospital for a period of one year. The participants belonging to age group of 20-60 years without any co-morbid conditions who provided informed consent and who were undergoing planned elective clean or clean-contaminated surgical procedures were included in the study. They were randomly assigned to study and control groups. The study group received a single dose of ceftriaxone 2g intravenously pre-operatively. The control group received 2g ceftriaxone intravenously post-operatively for three days. The participants were then followed up at regular intervals for the signs of SSI. The data was analysed using statistical software and chi-square test was used to assess the level of significance.

Results: A total of 100 participants were included in the study – 50 in the study group and 50 in the control group. The participants of both groups were similar in age, gender and type of surgery. Most common age group was 31-40 years of age with preponderance of male patients in both the groups. The most common surgery performed was hernioplasty (48% in study group & 44% in control group). Incidence of SSI was found to be 8% in the study group and 10% in the control group with an overall incidence of 9%. The most common organism isolated from SSI was Staphylococcus aureus. SSIs increased the overall duration of hospitalization (33.33%)and the rate of re-admission (33.33%).

Conclusion: Single dose of ceftriaxone pre-operatively is equally efficacious as the multiple dose post-operative ceftriaxone regimen for the prevention of SSIs in patients with clean or clean-contaminated surgeries.

Keywords: Antimicrobial prophylaxis, Ceftriaxone, Surgical site infection

I. INTRODUCTION

Surgical site infections (SSI) are classified as the infections which occur within 30 days of a surgical procedureand affects either the incision or deep tissue at the site of operation. If the surgical operation involved placing an implant, the duration is increased upto one year for the development of SSI.[1]SSIs can be superficial involving skin and subcutaneous tissues or it can be deep involving the deeper soft tissues like fascia and muscles. They may also involve deep spaces and organs, if severe or widespread.[1]According to theCentre for Disease Control National Nosocomial Infections Surveillance (CDC NNIS) system of United States, SSIs are the third most frequently reported nosocomial infections, with a prevalence of 38% among surgical patients and 14-16% in other hospitalised patients.[1, 2]SSIs are responsible for significant mortality and morbidity in the patients. They also contribute towards increased healthcare costs and adversely affect the quality of life of patients. Many studies in the past have evaluated the impact of SSI on patient outcomes

and healthcare costs. All of them have found that SSI increases the risk of readmission and reoperation, prolongs hospitalization, and increases mortality. [3, 4]A systematic review published recently also evaluated the available data on the cost of SSI on the healthcare system and concluded additional costs attributable to the investigation, treatment and medical staff employed.[5]Thus, it is imperative to effectively prevent the SSIs in post-operative period. Regular infection control practices such as use of sterile instruments and proper use of antiseptics and disinfectants to prevent cross-infection coupled with skilful surgical technique can help minimize the incidence of SSIs.

Antimicrobial prophylaxis is the use of antimicrobial agent (AMA) for the prevention of SSIs. However, there is rampant misuse of AMAs in this regard especially in developing countries, where surgeons do not rely much on the infection control practices like usage of sterile instruments and use of disinfectants and antiseptics.[6] This prolonged, extensive and often combined use of antibiotics practically in all the surgeries not only increases the chances of antimicrobial resistance, but also increases the financial burden for the patient as well as the healthcare providers.[7] Thus, systemic antibiotics should be used only when there is clear risk of SSI in any surgery. Usually, clean surgeries in otherwise healthy individual not suffering from any co-morbid conditions like diabetes, or is not otherwise immunocompromised does not require surgical prophylaxis in most cases.[6] It is very crucial to select an appropriate drug, dosage regimen, route of administration and duration of prophylactic antimicrobial according to individual patient and the type of surgical wound. There are various antibiotics which are used for surgical prophylaxis. Many studies in the past have showed that single dose of an antibiotic is often as effective as multiple doses of any antibiotic for the clean and clean-contaminated surgeries.[7-10] This study was done with an aim to help in the gradual shift from over dependence on AMAs for the prevention of SSIs especially in the clean and clean-contaminated surgeries. The objective of the study was to assess the efficacy of single dose pre-operative administration of Ceftriaxone versus post-operative three days regimen of ceftriaxone in patients undergoing elective surgeries which are clean or clean-contaminated ones.

II. METHODS

This was a randomized,prospective study carried out in the Department of Surgery of a Government Medical College, Rajkot a tertiary medical college from December 2017 to December 2018. The study was commenced after receiving permission from the Institutional Ethical Committee.

The following inclusion criteria were decided for recruitment of the study participants:

1. Patients with age 20-60 years belonging to both genders
2. Patients undergoing elective surgeries with no co-morbid conditions
3. Patients who provided written informed consent to be included in the study.

Following exclusion criteria were defined:

1. Patients who underwent emergency surgical procedures
2. Patients with minor or outpatient surgical procedures like endoscopy with less than 24 hours' length of hospital stay
3. Patients who had contaminated cavities like empyema, pyocele etc.
4. Patients with co-morbid conditions like malignancy or diabetes mellitus which predisposes to infection

Study procedure

After taking informed consent from the patients fulfilling the inclusion criteria of the study, they were randomly divided into two groups – study group and control group. For randomization, odd-even method was employed. The odd number of participants were allocated to the study group and the even number participants were allocated to control group. This ensured equal number of participants in both the groups randomly. All the relevant details about the patients such as demographic details, medical history and the details of the planned elective surgical procedure were taken.

All the participants in the study group received a single dose of injection ceftriaxone 2 gram intravenously at the time of induction of anaesthesia or 30 minutes prior to the skin incision. They were not given any further antibiotics orally or intravenously either during the operation or postoperatively. All the participantsin the control group received 2gram ceftriaxone intravenously post-operatively for three days. They did not receive any antibiotic preoperatively. The post-operative patients were monitored daily. They were observed for signs of systemic infections and a chart for vital signs was maintained. Wound dressing was opened on the third post-operative day and the incision site was examined for any sign of wound infection such as local erythema, inflammation, purulent discharge or raised temperature. This was again done on fifth, seventh,

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tenth, twentieth and thirtieth post-operative day. The total duration of follow up was up to six months.SSIs were defined using the following criteria:

- Presence of erythema or pus or inflammation diagnosed as SSI by the treating surgeon.
- Gross purulent discharge from the wound
- Spontaneous opening of the incision and drainage of purulent fluid
- Discharge positive for the presence of bacteria

The data was collected in a pre-approved data sheet and entered into Microsoft Excel 2016. The descriptive data was expressed in mean and percentages. Statistical analysis was performed using SPSS version 27. Chi square test was applied to compare the frequency of SSIs in two groups. P value < 0.05 was considered as significant.

III. RESULTS

A total of 100 participants were recruited for the study – 50 participants were allocated to study group and the other 50 were allocated to control group. They were subsequently subjected to the recommended surgical procedure after fulfilling all the necessary requirements pre-operatively. This was followed by post-operative care and routine follow up in outpatient department. In the study group, ceftriaxone was given prior to the surgery, while in the control group, it was given for three days post-operation.

After random allocation of participants to both the groups, they were matched for age, sex and type of surgery using frequency and chi-square test. This was to ensure no discrepancy in the result evaluation between the two groups. As depicted in table 1 the most common age group involved in both the study and control group was of 41-50 years of age. The mean age of patients in study group was 41 ±5.6 years and in control group was 46 ± 3.8 years. There was no significant difference between both the groups in terms of age distribution (P = 0.82). Table 2 shows the gender distribution of the patients in both the groups. Male participants were more common in both the study groups but there was no significant association with regards to the gender of the patients (P = 0.98).

Table 1. Age distribution of study participants (n = 100)

Age group (years)	Study group (n = 50)	Control group (n = 50)
21-30	5	9
31-40	16	14
41-50	21	20
51-60	8	7
P = 0.82		

Table 2. Gender distribution of study participants (n = 100)

Gender	Study group (n = 50)	Control group (n = 50)
Male	32	29
Female	18	21
P = 0.98		

Types of surgeries performed

Table 3 depicts the surgeries performed in patients of each group. The most common type of surgery performed was hernioplasty (48% in study group & 44% in control group) followed by Appendectomy (28% in study group & 32% in control group). The other surgeries that were performed were subtotal thyroidectomy, splenectomy, ureterolithiotomy etc. There was no significant discrepancy between the two groups of patients based on the type of surgeries (P = 0.87)

Table 3. Types of surgeries performed in study participants (n = 100)

Surgery	Study group (n = 50)	Control group (n = 50)
Hernioplasty	24 (48%)	22 (44%)
Appendectomy	14 (28%)	16 (32%)
Cholecystectomy	8 (16%)	6 (12%)
Others	4 (8%)	6 (12%)

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P = 0.87

Incidence of SSI

A total of 4 cases (8%) of SSI were reported among the study group who were given single dose pre-operative ceftriaxone and 5 cases (10%) of SSI were reported among the control group, who were given three doses of ceftriaxone post-operatively. The P value was 0.71. Hence, despite higher incidence rate in the control group, it cannot be conclusively said that the pre-operative antibiotic was more effective than post-operative antibiotic prophylaxis.

Type of organism involved

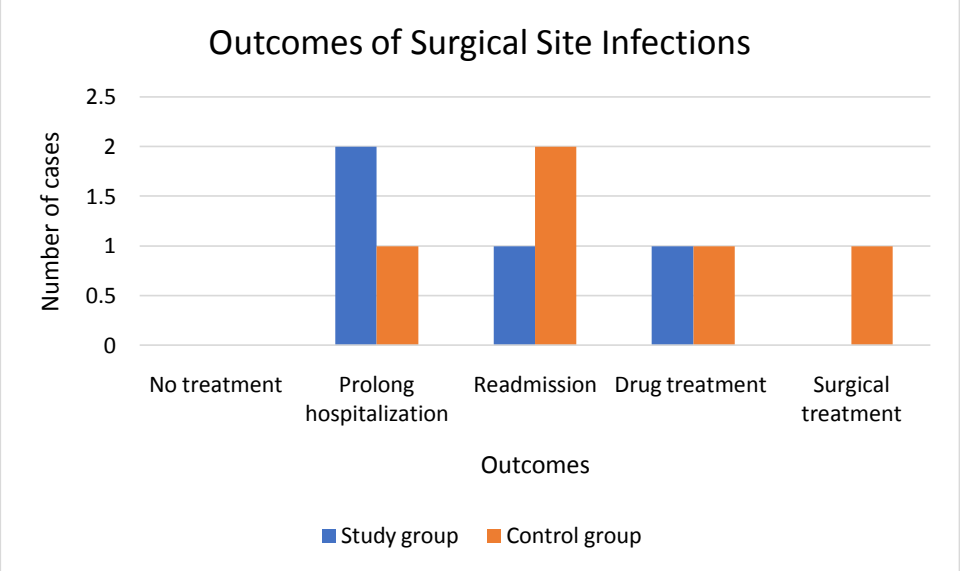
On culturing the discharge from the SSI, the microorganisms commonly involved in causing SSI were Staphylococcus aureus and Escherichia coli. (Table 4) This was similar in both the groups with no significant difference (P = 0.69).

Table 4. Microorganisms involved in surgical site infections (n = 9)

Microorganism	Study group (n = 4)	Control group (n = 5)
Staphylococcus aureus	3 (75%)	2 (40%)
Escherichia coli	1 (15%)	2 (40%)
Streptococcus	0 (00%)	1 (20%)
P = 0.69		

Outcome of SSI

Figure 1 depicts the outcomes of SSI in both the study and control group. All the SSIs in both the groups required some or other form of treatment. It either prolonged hospitalization of the patients, or led to re-admission in case of already discharged patients in both the groups. In one case of SSI among control group participants, minor surgical procedure to drain the abscess formed was required which was statistically significant (P = 0.034).



IV. DISCUSSION

SSI is one of the most common and feared of the post-operative complications. The incidence of SSI varies considerably ranging anywhere from 2.5% to 42% according to different studies.[11, 12] The incidence is believed to be quite less in clean and clean-contaminated surgeries as compared to the dirty contaminated wounds.[13] SSIs lead to significant impact on the patient's quality of life and increases healthcare expenditure of individual as well as healthcare providers. This makes SSI a grave public health concern. Antibiotic prophylaxis is usually employed to prevent SSIs. It usually differs according to the type of wound, type of surgery, patient status and presence of co-morbid conditions like diabetes. Different antibiotic regimens are available for prophylaxis. Careful selection of the appropriate drug regimen for an individual patient is pertinent for an effective antibiotic prophylaxis.[6] This study evaluated the

comparative efficacy of pre-operative single dose Ceftriaxone and post-operative three days treatment with Ceftriaxone, a third generation cephalosporin.

The study group and control group participants were similar when matched according to their age and gender. The most common age group was 41-50 years of age in both the groups. Also, there were more number of male patients as compared to female patients in both the groups. This was similar to the findings of the study conducted by Chandra Sekhar C[14] and Ranjan A et al.[15]

It was found that there was no significant difference between the study groups based on the types of surgeries performed. The most common surgery performed was hernioplasty followed by appendectomy and cholecystectomy. This was similar to the findings of Ranjan A et al.[15] and Abro A et al.[8]Thus, groups were similar in respect of the surgeries performed with hernioplasty being most common at 48% in study group and 44% in control group.

The overall incidence of SSI in the study participants was found to be 9% in our study (n = 9). The incidence of SSI in the study group was 8% and that in the control group was 10%. The difference was not statistically significant. Thus, though the incidence of SSI is lesser with a single dose pre-operative regimen of ceftriaxone, it cannot be convincingly ruled out that this could be due to chance. The findings of the incidence rate were similar to a recent study performed by Basant RK et al.[7] using 1 gram Cefotaxime intravenously pre-operatively single dose in study group and 1 gram Cefotaxime intravenously twice a day for five days post-operatively in the control group. The SSI incidence rate was found to be 6% in the study group and 8% in the control group depicting similar results. Also, similar comparative studies conducted in the past by Grazi GL et al.[16] and Chalkiadakis G et al.[17] using different regimens for Ceftriaxone pre-operatively and post-operatively have concluded similar findings of single pre-operative dose being equally effective to the post-operative multiple dose regimens for surgical prophylaxis in clean and clean-contaminated elective surgeries.

The microorganisms isolated from the infected wound were Staphylococcus aureus and Escherichia coli in study group. In control group, in addition to these two bacteria, Streptococcus was also isolated from one case. Thus, the most common infecting organism in the study participants was found to be Staphylococcus aureus (n = 5/9, 55.55%). These study findings are similar to the findings observed by the Basant RK et. al.[7] and Maciejczak A et al.[18]. The study performed by Maciejczak A et al. among a large cohort of spine surgery patients over a period of ten years found Staphylococcus aureus to be the most common causative organism in these patients.[18]

It was observed that the SSIs had a significant effect on the length of hospital stay of these patients. In our study, prolonged hospitalization was more common in study group (n =2, 50%) and re-admission due to SSI was more common in the control group (n = 2, 40%). Thus, an overall prolongation of hospitalization occurred due to SSI. This was similar to the findings observed in Basant RK et al.[7] and Syed N. et al[10]. This increase in the duration of hospital stay can in turn expose the patient to multiple other infections and also lower their immunity which can make them prone to acquiring infections in the hospital leading to an increase in the nosocomial infections. This will in turn increase the healthcare costs and affect the quality of life of the patient.[19]

There were a few limitations in our study. The most important one being we did not take into account other potential risk factors which can predispose a patient to SSIs for example, obesity and smoking. Also, we did not include the patients from other clinical surgical branches like Orthopedics, Gynecology and Obstetrics where surgery is routinely performed and SSIs can be common.

V. CONCLUSION

In conclusion, it can be said that the single dose pre-operative ceftriaxone is as effective as multiple dose post-operative ceftriaxone in patients undergoing clean or clean-contaminated surgery. Inadvertent, irrational and prolonged use of antibiotics will increase the incidence of antimicrobial resistance as well as healthcare costs for the patients and government. Thus, strategic planning to minimize the incidence of SSIs with judicious use of antimicrobials is the key to prevent SSIs in patients undergoing surgery. Further research comparing various drugs effective in the antimicrobial prophylaxis of SSI should be planned using different regimens and different routes of administration which can help in streamlining the use of antibiotics for surgical prophylaxis.

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