The comparative efficacy of prophylactic parenteral antibiotics with combined parenteral and pre-operative intra-incisional antibiotic administration in reducing surgical site infection

Dr. Singhvi Inderchand and Dr. Avinash Kulkarni

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Abstract
It has been proven to provide systemic cover by the absorption of the antibiotic from the incision site. This is primarily because the antibiotic gets fixed to the tissues along the incision and thus the antibiotic is present in a high concentration during time of maximum contamination of incision. Patient and/or his/her legally acceptable representative were explained about the study in detail and after obtaining their verbal consent for participation written voluntary informed consent was obtained. After obtaining the written consent the study related procedure was initiated. In Group 1, SSI was present in 7 (11.7%) patients and in Group 2 it was present in 1 (1.7%) patient. There was a significantly higher number of patients of SSI in group 1 in comparison to the Group 2 (P<0.05). In Group 1, 2 (3.33%) patients required resuturing, while in Group 2 none of the patients required any resuturing. There was statistically no significant difference in need for resuturing in both the groups (P>0.05).

Keywords: Prophylactic parenteral antibiotics, pre-operative intra-incisional antibiotic, surgical site infection

Introduction
Surgical site infection (SSI) continues to be a major problem since old time. It is one of the major causes for postoperative morbidity and mortality. Over the years, reasonable success has been achieved by taking various aseptic measures, which were initiated by Joseph Lister (1827–1912) in 1860. Initially, the antibiotics were only administered post-operatively for treatment of already established surgical site infection. Later, the concept of antibiotic prophylaxis was introduced. After administration of intravenous (IV) antibiotic, there is distribution of antibiotics, initially in the systemic pool and then in the peripheral pool, which results in a low concentration of the antibiotic at the site where it is needed the most [1].

Therefore, the search for alternative modes of administration of prophylactic antibiotics was started so as to affect a further decrease in the rate of wound infection. One such method is the intra-incisional infiltration of prophylactic antibiotics [2, 3]. This mode ensures a high concentration of antibiotic at the incision site and immediate effective levels. Conversely IV, IM or oral administration requires a significant delay to attain effective levels of an antimicrobial in tissue. It has been proven to provide systemic cover by the absorption of the antibiotic from the incision site. This is primarily because the antibiotic gets fixed to the tissues along the incision and thus the antibiotic is present in a high concentration during time of maximum contamination of incision. Intra incisional administration may also offer advantages with reducing exposure of other body sites to antibiotics [4].

Methodology
Patient and/or his/her legally acceptable representative were explained about the study in detail and after obtaining their verbal consent for participation written voluntary informed consent was obtained. After obtaining the written consent the study related procedure was initiated. A detailed history and clinical examination of the cases were done. Routine preoperative investigations were done. All the patients were admitted one day prior to operation day, preoperative showers was given with simple detergent soap.
Parts preparation (hair removal) was done by clipping method 1 hour before the surgery. Sterilization of instruments was done by standard Autoclave method. Skin was prepared by 5% chlorhexidine scrub and 10% povidone iodine solution. Standard draping technique was used with usage of surgical face mask, gowns and haircap for surgeon in all cases. All hand Jewellery, artificial nails (if present) were removed. Surgeons hand/forearm antisepsis was done with 5% chlorhexidine scrub and alcohol solution. Surgical skin incision was done by standard number 20 surgical blade in all patients and skin was approximated either by stapler or simple suture or vertical mattress suture using Nylon thread. Further wound dressings were done by povidone iodine ointment and cotton gauze by no touch technique. A single dose of 1.5 gram of Cefoperazone+sulbactum with 100ml normal saline was administered intravenously 20 minutes before the surgical incision at the time of induction of anesthesia. Prophylaxis by both intravenous and intra-incisional infiltration of the antibiotic (1.5 gram of Cefoperazone+sulbactum was administered intravenously and 1.5 gram of Cefoperazone+sulbactum diluted in 10 to 15 ml of distilled water was infiltrated along the site of proposed incision 20 minutes before incision).

Injection was carried out using a 22-French Quincke type point spinal needle subcutaneously (and often, in thin patients, intramuscularly) along the line of the proposed abdominal incision, with a careful attempt being made to perform uniform infiltration along the incision. The wounds were an average of 5 to 15 centimeter long; thus approximately 1 to 2 ml of antibiotic solution was injected along each centimeter. Choice of anesthesia was dependent on surgeon and the anesthetist. The results were analyzed statistically.

Procedure of data collection
Data for the patient study was collected in a customized proforma specially designed for the study.

Outcome measures
The following parameters viz. days of hospitalization, cost of the treatment, requirement of re-suturing/dressings, usage of other antibiotics (according to Culture/Sensitivity from wound) was formed for the outcome measures.

Statistical analysis
Data from the study proforma was transferred to MS excel and then later transferred to statistical software IBM-SPSS version 20.0.0 for analysis.

The mean comparison was done using unpaired T test. The proportional comparison was done using Z test and chi-square test for two sample proportions. The P value of <0.05 was taken as statistically significant.

Ethical/legal considerations
Synopsis of the present study was being submitted to the ethics and scientific review committee of Choithram Hospital and Research Centre, Indore for evaluation and approval. After getting their approval study was initiated in the institute. Before performing the study related procedure written informed consent was obtained from the patient and/or his/her legally acceptable representative. This consent was taken in addition to the other consent that were obtained for the management of the disease as per the laid down norms of the institute.

Results

Table 1: Comparison of mean hospital stay (days)

| Hospital Stay (Days) | Group 1 (n=60) [Mean±SD] | Group 2 (n=60) [Mean±SD] |
|----------------------|--------------------------|--------------------------|
| Mean ± SD (Days)     | 3.33 ± 0.63              | 3.10 ± 0.30              |
| 't' Value            | 2.59, df=118             | 0.011*                   |
| P Value              |                          |                          |

Unpaired ‘t’ test applied. P = 0.011, Significant

The above table shows the comparison of mean hospital stay in both the groups. In Group 1, the mean hospital stay was 3.33 ± 0.63 days, while in Group 2, it was 3.10 ± 0.30 days. The hospital stay in Group 1 was more in comparison to the Group 2 and which was statistically significant (P<0.05).

Table 2: Comparison of mean postoperative RBS

| RBS        | Group 1 (n=60) [Mean±SD] | Group 2 (n=60) [Mean±SD] |
|------------|--------------------------|--------------------------|
| Mean ± SD (mg/dL) | 118.6 ± 11.0             | 114.75 ± 9.95            |
| 't' Value   | 1.99, df=118             | 0.049*                   |
| P Value     |                          |                          |

Unpaired ‘t’ test applied. P = 0.049, Significant

The above table shows the comparison of mean postoperative RBS in both the groups. In Group 1, the mean postoperative RBS was 118.6 ± 11.0, while in Group 2 it was 114.75 ± 9.95. Mean postoperative RBS was higher in Group 1 in comparison to Group 2 (P<0.05).

Table 3: Comparison of mean number of dressings

| Dressings (No.) | Group 1 (n=60) [Mean±SD] | Group 2 (n=60) [Mean±SD] |
|-----------------|--------------------------|--------------------------|
| Mean ± SD (No.) | 2.77 ± 0.79              | 2.58 ± 0.62              |
| 't' Value       | 1.42, df=118             | 0.159                    |
| P Value         |                          |                          |

Unpaired ‘t’ test applied. P = 0.159, Not significant

The above table shows the comparison of mean number of dressings in both the groups. In Group 1, the mean number of dressings was 2.77 ± 0.79 while it was 2.58 ± 0.62 in Group 2. The mean number of dressings in both the groups were comparable (P>0.05).

Table 4: Distribution according to SSI

| SSI       | Group 1 (n=60) | Group 2 (n=60) |
|-----------|----------------|----------------|
| No.       | %              | No.            | %              |
| Absent    | 53             | 88.3           | 59             | 98.3           |
| Present   | 7              | 11.7           | 1              | 1.7            |
| Total     | 60             | 100.0          | 60             | 100.0          |

χ²=4.821, df=1, P value = 0.028, Significant

The above table shows the distribution of patients according to SSI. In Group 1, SSI was present in 7 (11.7%) patients and in Group 2 it was present in 1 (1.7%) patient. There was a significantly higher number of patients of SSI in group 1 in comparison to the Group 2 (P<0.05).

Table 5: Comparison of Culture and Sensitivity Findings

| Culture and Sensitivity Findings | Group 1 (n=60) | Group 2 (n=60) | Z Value | P Value |
|----------------------------------|----------------|----------------|---------|---------|
| No growth                        | 53             | 88.3           |         |         |
| Growth seen                      | 7              | 11.7           |         |         |
| Total                            | 60             | 100.0          | 60      | 100.0   |

Z test for two sample proportion. P = 0.025, Significant
The above table shows the comparison of culture and sensitivity findings in both the groups. In Group 1, growth was seen in 7 patients. 1 (1.7%) patient had E. coli, 1 (1.7%) patient had pseudomonas and 5 (8.3%) patients had staphylococcus MRSA. In Group 2, only 1 (1.7%) patient had staphylococcus MRSA growth. In Group 2 majority of the patients did not have any growth on culture. Larger proportion of patients in Group 1 showed growth of organism in comparison to the Group 2, which was statistically significant (P>0.05).

**Table 6: Distribution according to need for resuturing**

| Resuturing | Group 1 (n=60) | Group 2 (n=60) |
|------------|----------------|----------------|
| No         | 58             | 60             | 100.0          |
| Yes        | 2              | 0              | 0.00           |
| Total      | 60             | 60             | 100.0          |

χ²=2.034, df=1, P value = 0.154, Not significant

The above table shows the comparison need for resuturing in both the groups. In Group 1, 2 (3.3%) patients required resuturing, while in Group 2 none of the patients required any resuturing. There was statistically no significant difference in need for resuturing in both the groups (P>0.05).

**Table 7: Distribution according to additional antibiotics requirement**

| Additional Antibiotics Requirement | Group 1 (n=60) | Group 2 (n=60) |
|-----------------------------------|----------------|----------------|
| No                                | 56             | 59             | 98.3           |
| Given                             | 4              | 1              | 1.7            |
| Total                             | 60             | 60             | 100.0          |

χ²=1.878, df=1, P value = 0.171, Not significant

The above table shows the need for additional antibiotics requirement in both the groups. In Group 1, additional antibiotics were given in 4 (6.7%) patients and in Group 2, additional antibiotics were given in 1 (1.7%) patient. There was statistically no significant difference in need for additional antibiotics requirement (P>0.05).

**Discussion**

In our study we found that In Group 1, the mean postoperative RBS was 118.6 ± 11.0, while in Group 2 it was 114.75 ± 9.95. Mean postoperative RBS was higher in Group 1 in comparison to Group 2 (P>0.05). The mean postoperative RBS of Group 1 was nearly comparable with one case of Group 2. Similarly Latham et al. [3] found that Diabetes (odd ratio [OR], 2.76; P>0.001) and postoperative hyperglycemia (OR, 2.02; P=0.007) were independently associated with development of SSIs. Also in a univariate analyses by Waisbren et al. [6], significant predictor of SSI was postoperative hyperglycemia (P = 0.03). The odds ratio for developing a wound complication was 3.75 (95% confidence interval, 1.25 to 11.22; p = 0.02) in patients with a mean postoperative glucose of >200 mg/dL, 3.0 (95% confidence interval, 0.97 to 9.30; p = 0.08) in patients with a maximum postoperative blood glucose of >260 mg/dL, and 9.0 (95% confidence interval, 1.14 to 71.20; p = 0.03) in patients with a preoperative hemoglobin A1C value of >6.7% found by Styrker et al. [7].

In our study we found that in Group 1, the mean number of dressings was 2.77 ± 0.79 while it was 2.58 ± 0.62 in Group 2. The mean number of dressings in both the groups were comparable. (P>0.05). Similarly Dumville et al. [6] did a Cochrane based study in which no evidence was identified to suggest that any dressing significantly reduced the risk of developing an SSI compared with leaving wounds exposed or compared with alternative dressings in people who had surgical wounds healing by primary intention. Similarly in a meta-analysis done by Walter et al. [9] found no evidence that any dressing significantly reduced surgical-site infection rates compared with any other dressing or leaving the wound exposed. So also in a Cochrane based study by Toon et al. [10] showed that there were no statistically significant differences between the early dressing removal group and delayed dressing removal group in the proportion of people who developed superficial surgical site infection within 30 days (RR 0.64; 95% CI 0.32 to 1.28), superficial wound dehiscence within 30 days (RR 2.00; 95% CI 0.19 to 21.16) or serious adverse events within 30 days (RR 0.83; 95% CI 0.28 to 2.51).

In our study we found that in Group 1, SSI was present in 7 (11.7%) patients and in Group 2 it was present in 1 (1.7%) patient. There was a significantly higher number of patients of SSI in group 1 in comparison to the Group 2 (P>0.05). Similar study by Dogra et al. [11] found that there was also significant reduction in incidence of SSI in the group, which received both intra incisional and intravenous antibiotic (2.5%) preoperatively than the patients who received only intravenous (10%) and only intra incisional (18%) antibiotic. So also study by Pollock et al. [12] showed The incidence of wound infections was considerably lower in the group which received the antibiotic into the abdominal wall (8.4% compared with 15.9%--chi 2 = 7.90, P = 0.005). Another study by Pollock et al. showed there was no significant differences between the two groups in the rates of major (3.5% and 2.1%) or minor (12.4% and 15.5%) wound sepsis incidence. Taylor et al. [13] found that there was one wound infection in the group treated with preoperative intracisional administration of cefamandole whereas 18 occurred in the control patients with no antibiotic (P>0.001). Dixon et al. found a significant reduction in the frequency of wound infections in patients receiving preincisional antibiotics over intravenous and group with no antibiotic. Grego et al. found that 2.5% of SSI occurred in the group with no antibiotic, while only 0.2% occurred in the nafcillin group. This difference was highly significant (P = .003).

Also in Group 1, additional antibiotics were given in 4 (6.7%) patients than in Group 2, in 1 (1.7%) patient. But there was statistically no significant differences in need for additional antibiotics requirement (P>0.05). Given the absence of any evidence on efficacy and safety, this practice cannot be recommended to date, and it should be definitely be banned for aminoglycosides. However, it may deserve further research for time-dependent antibiotics because it could offer several advantages compared to other parenteral routes, especially Cephalosporins. But we could not find any study pertaining with subcutaneous administration of SBT/CPZ in reducing SSI as far as our knowledge is concerned.
But in an animal study they found that: Plasma elimination half-life after parenteral administration in mouse, rat, rabbit, dog, monkey and man was 8 to 120 minutes. No significant differences were seen in plasma elimination half-life between intramuscular, intravenous, subcutaneous and intraperitoneal administration. To compare the efficacy and safety of intramuscular cefoperazone and intramuscular ceftriaxone in the treatment of nursing home-acquired pneumonia in the nursing home setting and concluded, Intramuscular cefoperazone and intramuscular ceftriaxone are safe and effective in the treatment. The advantages of the combination of cefoperazone plus sulbactam over cefoperazone alone include a prolonged half-life, a prolonged postantibiotic effect, and a broadened spectrum of activity against microorganisms, including gram-negative bacilli, gram-positive cocci, and anaerobes. The combination of cefoperazone plus sulbactam has been shown to be clinically effective in the treatment of infections in immunocompetent hosts as well as those with concomitant hematologic malignancies [14] As SBT/CPZ was choosen in regard with similar studies present with cephalosporins and SBT/CPZ has long half life (single dose justified within 24 hrs) and also because of its known effectiveness against a wide range of wound pathogens, including obligate anaerobes, at concentrations likely to be present locally. The simultaneous measurement of serum, wound tissue edges, and wound fluid antibiotic concentration of SBT/CPZ in the risk of infection patients undergoing surgery has not been reported, to our knowledge.

**Conclusion**

Prevention of SSI is a fundamental basis of perioperative period. After this study we can conclude that both intra incisional and intravenous antibiotic administration is better in reducing surgical site infection as compared to only intravenous. The development of a complication in the form of SSI prolongs the patient’s hospitalization and increases the hospitalisation costs. This can also reduce the patient’s morbidity (requirement of additional antibiotics, resuturing).

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