

# Single Dose versus 24 - Hours Antibiotic Prophylaxis against Surgical Site Infections

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## ABSTRACT

**OBJECTIVE:** To observe the effect of single dose antibiotic is it as efficient as a 24-hour regimen in preventing SSIs in adults undergoing clean, clean contaminated and contaminated elective surgical procedures.

**STUDY DESIGN:** Random, prospective

**SETTING AND DURATION:** Department of general Surgery, Liaquat University Hospital, Jamshoro, Pakistan from May 2011 to April 2012

**PATIENTS AND METHODS:** A total of 208 patients undergoing general surgical operations were included in the study. The patients were randomly divided into two groups. The single-dose group received 2 grams of ceftriaxone intravenously, whereas the 24-hour group received 2 grams of ceftriaxone intravenously at the time of induction of anaesthesia, followed by 1 g at 8 and 16 hours postoperatively.

**RESULTS:** The administration of ceftriaxone in a single dose regimen was associated with higher rate of SSIs compared with rates for patients receiving the 24-hour regimen (9.6% vs. 6.7%).

**CONCLUSION:** Multiple doses of prophylactic antibiotics over 24 hours should be used instead of single doses in surgical prophylaxis in clean-contaminated and contaminated procedures.

**KEYWORDS:** Surgical Site Infection (SSI), Antibiotic Prophylaxis.

## INTRODUCTION

Surgical site infections (SSIs) remain a global issue. They are the third most commonly reported nosocomial infection<sup>1</sup> and account for over a fifth of all health-care associated infections.<sup>2</sup> SSIs are not only responsible for increasing financial burden on the hospital and patients but are also a major cause of postoperative morbidity and mortality.

The benefits of pre-operative antimicrobial prophylaxis in preventing SSTs have been clearly demonstrated.<sup>3,4</sup> Most surgical centers recommend multiple-dose antibiotic prophylaxis that continues for 24 to 48 hours and often until all the drain tubes are removed.<sup>5</sup> Inappropriate use of antimicrobials in surgical chemoprophylaxis leads to higher surgical site infection rate.<sup>6</sup> Injudicious use of antibiotics is also associated with increased costs, unwanted drug side effects as well as the emergence of resistant strains and multidrug resistant infections. In recent years, there has been an increased interest in the potential clinical benefits of administering the antibiotic as a single dose. There is ample evidence of efficacy, cost effectiveness and safety of single dose prophylaxis in the literature;<sup>7,8</sup> it is reported to be associated with reduced antibiotic associated resistance, and fewer problems with drug toxicity and superinfections. However, there is no consensus on the type of antibiotic prophylaxis, whether a single dose or multiple doses

should be used.<sup>9, 10</sup>

Our hospital practice of antibiotic prophylaxis includes preoperative antibiotic followed by 24-hour postoperative antibiotics. Most surgeons in Hyderabad are reluctant to use single dose prophylaxis in clean, clean contaminated and contaminated operations for variable reasons, including skepticism for optimum sterilization techniques in both public and private hospitals. The aim of this study was to test the hypothesis that single dose antibiotic is as effective as a 24-hour regimen in preventing SSIs in adults undergoing clean, clean contaminated and contaminated elective surgical procedures. The purpose was to reduce the use of antibiotics and to develop best guidelines for antibiotic prophylaxis in clean-contaminated and contaminated general surgical procedures.

## PATIENTS AND METHODS

This random, prospective study was conducted between May 2011 and April 2012 in the Liaquat University Hospital, Jamshoro, Pakistan after due approval from the Institutional Ethics Review Committee.

All adult patients, above 18 years of age, scheduled for elective clean, clean contaminated and contaminated general surgical procedures were initially included in the study. 246 patients were enrolled in the study, and 38 were excluded due to default on antibiotic prophylaxis or lost to follow-up. A clean contaminated wound

is defined as a wound with transection of the gastrointestinal, respiratory, or genitourinary tracts without significant spillage of the contents. A clean surgery with a minor break in the sterile technique also comes under this category. Due to lack of modern sterilization technique and poor training of the theatre staff in sterilization techniques, all clean surgeries in our series were considered as clean contaminated. A contaminated wound is defined, as one in which there is transection of the gastrointestinal, respiratory, or genitourinary system with significant spillage of the contents. Patients with active infection, those already on antibiotics for unrelated diseases, emergency surgical procedures and those who did not wish to be a part of the study were excluded from the study. Patients with comorbidities like diabetes mellitus, anaemia, malignancy etc. were also excluded from the study. Informed consent was obtained from all those who participated in the study.

The patients were randomly divided into two groups using sequential method. The single-dose group received 2 grams of ceftriaxone (Getofin®) intravenously at the time of induction of anaesthesia, whereas the 24-hour group received 2grams of ceftriaxone (Getofin®) intravenously at the time of induction of anaesthesia, followed by 1g at 8 and 16 hours post-operatively. Where procedures involved opening of the gastrointestinal or genitourinary tracts, metronidazole 500mg and gentamycin 120 mg was added respectively. All patients were operated on elective list. The operative site was shaved in the theatre, skin was prepared with povidone iodine and sterile drapes were applied to isolate the operative area. All wounds were closed either with subcuticular or interrupted prolene sutures or with staples and were dressed with sterile gauze. No pre-packed sterile dressing was used in any patient.

From the 4th postoperative days onward, until the day of discharge, patients were examined daily by one researcher, with a follow up of up to 35 days after surgery. Pain at the operative site, persistent fever >38° C, wound erythema, tenderness, wound discharge and dehiscence were taken as signs of SSI. All patients developing SSI were started on empirical antibiotic therapy awaiting results of bacterial culture and sensitivity from wound discharges. Discharge from the hospital was determined on the basis of the nature of surgery and varied from 24 hours to 8 days.

All analyses were conducted using the SPSS® for windows version 11.0. Both groups were compared using chi-square test. All p-values were two sided and considered as statistically significant if <0.05.

**RESULTS**

Over the study period, 246 patients were enrolled in

the study, and 38 were excluded for defaulting on the randomized prophylactic antibiotic regimen or being lost to follow-up. A total of 208 patients completed the study. There were 97 males and 111 females. The mean age was 34.7 years (range 18 to 69 years). 104 patients received single doses of ceftriaxone and 104 received 24-hour regimen. Both groups were homogeneous and comparable as far as their demographic profiles and clinical characteristics were concerned.

Of the 208 patients, 17 (8.2%) presented with SSIs. A total of 10 SSIs (9.6%) were documented in the single-dose group and 7 (6.7%) in the 24-hour group (p = .004). All SSIs were either superficial or deep incisional in either group with no organ space SSI recorded in any patient. Table I shows surgical procedures carried out and the respective infection rate. Table II shows the breakup of infections in the two groups.

**TABLE I: INFECTION RATES IN VARIOUS SURGERIES (n=208)**

Operations Performed	No. Performed (%)	No. Infected (%)
<b>Clean contaminated</b>		
Inguinal hernioplasty	36 (33.3)	1 (5.8)
Laparoscopic cholecystectomy	32 (15.4)	2 (11.7)
Firoadenoma	31 (14.9)	0 (0)
Open cholecystectomy	21 (10.9)	1 (5.8)
Subtotal thyroidectomy	15 (7.2)	1 (5.8)
Excision of lymph nodes / Sebaceous cyst / ganglion / lipoma	15 (7.2)	0 (0)
Appendicectomy	13 (6.2)	3 (17.6)
Flush ligation / stripping of great saphenous vein	03 (1.4)	0 (0)
Ureterolithotomy	03 (1.4)	1 (5.8)
Pleomorphic adenoma	02 (0.9)	0 (0)
Splenectomy	02 (0.9)	0 (0)
Nephrectomy	01 (0.5)	0 (0)
Tracheostomy	01 (0.5)	0 (0)
<b>Contaminated</b>		
Right hemicolectomy	09 (4.3)	5 (29.4)
Resection and anastomosis	08 (3.8)	2 (11.7)
Exploratory laparotomy	08 (3.8)	0 (0)
Pyelolithotomy	06 (2.8)	1 (5.8)
Gastrojejunostomy	02 (0.9)	0 (0)

**TABLE II: DISTRIBUTION OF INFECTIONS ACCORDING TO THE ANTIBIOTIC REGIMEN**

Procedure	Single Dose antibiotics (n=10)	24-hour antibiotics (n=07)
Inguinal hernioplasty	1	-
Laparoscopic cholecystectomy	1	1
Open cholecystectomy	1	-
Subtotal thyroidectomy	1	-
Appendectomy	2	1
Ureterolithotomy	-	1
Right hemicolectomy	3	2
Resection & anastomosis	-	2
Pyelolithotomy	1	-
<b>Total</b>	<b>10 (9.6 %)</b>	<b>07 (6.7 %)</b>

The pathogens isolated in the SSIs were similar in the two groups ( $p \geq .05$ , Table III). In 8 (47%) of the 17 patients who developed SSIs, the organisms were gram –positive cocci. The most frequently isolated microorganism was Staphylococcus epidermidis. Gram -negative bacilli caused 29.5% (5/8 cases) of the SSIs while polymicrobial infection was found four (23.5%) patient belonging to the 24-hour regimen group.

**TABLE III: FREQUENCY OF VARIOUS PATHOGENS CAUSING SURGICAL SITE INFECTION**

Organisms	No. of isolates (%)
Staphylococcus epidermidis	6 (35.3)
Staphylococcus aureus	2 (11.7)
E. coli	3 (17.6)
Proteus	2 (11.7)
Mixed infection	4 (23.5)

(n=17)

**DISCUSSION**

Surgical Site infection (SSI) remains an important cause of postoperative complications. Its incidence varies widely worldwide from 2.5% to 41.9%.<sup>11-14</sup> The overall surgical site infection rate in the present study was 8.2%. The optimum duration of antibiotic prophylaxis remains controversial. Various regimes range from single dose to multiple doses for several days.<sup>15</sup>

<sup>16</sup>Contrary to the general consensus of postoperative antibiotics for 24 hours in clean contaminated and contaminated cases, we believe that single dose regime is as effective as 24-hour regime in the prevention of SSIs.

The role of prophylactic antibiotic therapy in un-perforated appendicitis is still controversial.<sup>17,18</sup> Nooyen et al. in their study comparing single dose and a 3-day course of prophylactic antibiotics concluded that a single dose of prophylactic antibiotic is as effective as a 3-day course in the prevention of SSI.<sup>19</sup> Eduardo et al. in their randomized prospective, clinical study, conducted in 1027 patients undergoing cardiac surgery, verify that single doses of prophylactic antibiotics are as effective in preventing SSIs as 24 -hours of antibiotics.<sup>20</sup> In this study, 104 patients received single doses of ceftriaxone at the induction of anaesthesia. Another group of 104 patients received three doses of prophylactic antibiotics, at the time of induction of anaesthesia and at 8 and 16 hours post-operatively. The administration of ceftriaxone in a single dose regimen was associated with higher rate of SSIs compared with rates for patients receiving the 24 -hour regimen (9.6% vs 6.7%).

The study confirms that gram-positive cocci, especially S epidermidis, followed by S aureus are the commonest organisms causing SSIs. These findings are supported by other similar studies, which confirm gram-positive organisms responsible for majority of SSIs world over.<sup>21</sup> Hence, prophylactic antibiotics in clean and clean contaminated surgeries, not violating integrity of gut should preferably be against skin organisms. However, procedures involving opening up of GIT, biliary tract or urinary tract should include at least second-generation cephalosporin.

This randomized, prospective study was conducted to verify the hypothesis that single dose antibiotic is as effective as 24-hour regimen in reducing SSI in adult patients undergoing elective clean-contaminated and contaminated general surgical procedures. The two groups were homogenous in their demographic and clinical specifications. Although several studies conducted in Europe and United States of America suggest that effective wound infection prophylaxis can be achieved with a single dose of antimicrobial, we found a higher rate of SSIs in patients receiving single prophylactic dose of ceftriaxone as compared to those receiving 24-hour dose regimen. Timing of administration of antibiotics is the most important factor responsible to cause SSIs; too early or too late antibiotic ad-

ministration produces inadequate concentration of drug in tissues at the operative site, resulting in bacterial proliferation.<sup>22</sup> The antibiotics should therefore be given at the time of induction of anesthesia, repeating a dose if the surgery lasts more than four hours.

## CONCLUSION

We conclude that multiple doses of prophylactic antibiotics over 24 hours should be used instead of single doses in surgical prophylaxis in clean-contaminated and contaminated procedures.

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