*Original Article*

# A Prospective Study Comparing Single with Multiple Antibiotic Prophylaxis Dose in Elective Cholecystectomy

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## ABSTRACT

**Background:** Cholecystectomy is one of the commonest, clean and contaminated surgery operations performed by the surgeons worldwide. Antibiotic prophylaxis in elective cholecystectomy is a controversial issue and our study was undertaken to evaluate the rate of infection and the usefulness and efficacy of antibiotic prophylaxis in elective cholecystectomies. **Methods:** The study comprised of 100 patients admitted for elective cholecystectomy. The first fifty patients undergoing elective cholecystectomy were given the prophylactic antibiotic outside the operation theater in the wards and the next fifty patients were given a single dose of injection cefuroxime (1.5 gm i.v). **Results:** In single dose antibiotic prophylaxis group 10.52% people developed surgical site infection in open cholecystectomy group while patients developed infection in laparoscopic cholecystectomy group but in multiple dose group 16.21% patients who underwent open cholecystectomy developed a surgical site infection while 10% developed an SSI in laparoscopic cholecystectomy group. In both the groups, results are statistically not significant. **Conclusion:** This study document that one single dose of prophylactic antibiotic, administered at induction of anaesthesia, is sufficient to prevent post-operative infective complications in patients undergoing elective cholecystectomy.

Key words: Antibiotic Prophylaxis, Cephalosporin, Elective Cholecystectomy

## INTRODUCTION

A surgical site infection (SSI) is defined as an infection that occurs at or near a surgical incision within 30 days of the procedure or within one year if an implant is left in place. In the twentieth century, the two key factors that have enabled surgical advances, such as open heart surgery and kidney transplants, to become routinely possible and safe are improved anesthesia and scientifically sound infection prevention practices. Despite improvements in operating room practices, instrument sterilization methods, better surgical technique and the best efforts of infection prevention practitioners, SSI remain a major cause of nosocomial (hospital-acquired) infections—and rates are increasing globally.[1]

The Centre for Disease Control and Prevention (CDC) estimates that approximately 500,000 SSI occur annually in the United States.[2] They are the leading cause of nosocomial infections after surgery, accounting for nearly 40 percent of nosocomial infections in surgical patients.[3]

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Furthermore, patients who develop surgical site infections are five times more likely to be readmitted to the hospital, 60 percent more likely to spend time in the intensive care unit, and twice as likely to die compared with surgical patients without the infections.[4]

Cholecystectomy is one of the commonest operations performed by the surgeons worldwide. It being a clean contaminated surgery, use of prophylactic antibiotics (a brief course of an antimicrobial agent administered just before an operation) is mandatory to decrease the incidence of surgical site infections.[3] In many trials worldwide it has been established that the single dose of prophylactic antibiotics is as effective as the multidose regimens. But still out of undue fear of surgical site infections the prophylactic antibiotics are being misused and continued for many days in post operative period adding to the cost burden to the patients as well as drug resistance in the microbes. To reduce the risk of nosocomial SSIs in developing countries, a systematic but realistic approach must be applied with awareness that this risk is influenced by characteristics of the patient, the operation, the healthcare staff and the hospital. Our study aims to observe the surgical site infection rate in patients who are administered single dose prophylactic antibiotics.

## MATERIALS AND METHODS

This study was conducted in the Department of surgery at Dr RPGMC (Tanda) from October 2012 to July 2013 after the approval from the college ethics committee. The patients admitted for elective laparoscopic cholecystectomy, aging less than 65 yrs of both the genders were included. Patients with co-morbid conditions like diabetes mellitus, jaundice, uremia, hypertension, neoplasia, cardiac or renal disease, immunosuppressed patients, pregnant, lactating women, patients on antibiotic therapy, Cephalosporins allergy, Conversion to open cholecystectomy and patients with infective focus in the body were excluded from the study.

After admission, detailed history, examination and basic investigations were performed for all subjects. All the participants gave their written informed consent after they had been made aware of the purpose of the study.

The study comprised of 100 patients admitted for elective cholecystectomy. The first fifty patients undergoing elective cholecystectomy were given the prophylactic antibiotic outside the operation theater in the wards and the antibiotics were continued for a variable period of time. The next fifty patients were given a single dose of injection cefuroxime 1.5 gm i.v. after the test dose just before the induction of anaesthesia. Another dose of the antibiotic was given in case of the procedures lasting longer than two hours.

The surgical site was prepared inside the operation theater. Two coats of 7.5% betadine paint were applied to the skin. The standard aseptic precautions were followed at each step. Post-operatively the wounds were examined on second day, time of discharge; the sutures were removed in outpatient department (OPD) on ninth post operation day. After that the patients came for follow up in OPD on 30th post op day.

**Statistical Analysis:** The data was subjected to descriptive analysis. Mean and range were determined from continuous data. Student's t-Test was applied to continuous variables and chi square and Z-test for two independent proportions were applied to categorical data.

## RESULTS

We enrolled 100 patients admitted for elective laparoscopic cholecystectomy from October 2012 to July 2013. Doses of antibiotics to the patients were given as per study protocol. All the precautions were taken to ensure asepsis at different levels of the surgery during both the periods. Three patients were lost to follow up and 3 others were excluded because of Hepatitis B, Hypothyroidism and Hypertension. Demographic data were comparable in both the groups [Table 1].

**Table 1:** Age and. Sex distribution.

| Antibiotic regimen | 11-20 (years) | | 21-30 (years) | | 31-40 (years) | | 41-50 (years) | | 51-60 (years) | | 61-65 (years) | | Total | Average age | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | M | F | M | F | M | F | M | F | M | F | M | F | | M | F |
| Single dose (n=47) | 0 | 0 | 1 | 6 | 1 | 19 | 1 | 11 | 1 | 5 | 0 | 2 | 47 | 38.75 | 41 |
| Multiple dose (n=47) | 0 | 1 | 1 | 9 | 1 | 16 | 1 | 7 | 1 | 9 | 0 | 1 | 47 | 41.5 | 41.2 |

In the single dose antibiotic prophylaxis group 10.63% surgical site infections were noticed in comparison to multiple dose antibiotic group where 14.89% surgical site infections were noticed. Overall 12.76% surgical site infections were noticed [Table 2]. During our study, 50% superficial SSI, 33.33% deep SSI and 16.67% organ space SSI were noted out of all SSIs. However, the incidence of superficial SSI as well as deep SSI was same (4.25%) in case of single dose group whereas in multiple dose group, incidence of superficial SSI was 8.51% [Table 3]

**Table 2:** Distribution of Infection Rates

| Dosage regimen | Infection | Without infection | Percentage |
|---|---|---|---|
| Single dose | 5 | 42 | 10.63 |
| Multiple dose | 7 | 40 | 14.89 |
| Total (94) | 12 | 82 | 12.76 |

**Table 3:** Type of Infection In Both Groups

| Type of SSI | Superficial SSI | Deep SSI | Organ/space SSI |
|---|---|---|---|
| Single dose (47) | 2 | 2 | 1 |
| Multiple dose (47) | 4 | 2 | 1 |
| Total (94) | 6 | 4 | 2 |

In single dose antibiotic prophylaxis group 10.52% people developed SSI in open cholecystectomy group while 11.11% patients developed infection in laparoscopic cholecystectomy group [Table 4] but in multiple dose group 16.21% patients who underwent open cholecystectomy developed a SSI while 10% developed an SSI in laparoscopic cholecystectomy group [Table 4]. In single dose group and multiple dose group the mean pre operative hospital stay was 2.32 days (1-6 days) and 1.91 days (1-3 days) respectively. In single dose group 32 (68.08%) patients and in multiple dose group 43 (91.5%) patients had a pre operative hospital stay of 2 or less number of days. Two patients developed infection that had a pre operative hospital stay of 1-2 days in single dose group and in multiple dose group 7 patients had SSI in 0-2 days preoperative hospital stay group [Table 5]. The mean post op hospital stay in single dose group and multiple dose group was 2.1 days (1-7 days) and 2.83 days (1-5 days) respectively [Table 6]. The mean duration of hospital stay for the patients in single dose group and multiple dose group was 4.46 days (3-9 days) and 4.96 days (3-7 days) respectively [Table 7].

**Table 4:** Type of Surgery Vs. Infection Rates In Single Dose Antibiotic Group

| Variables | Single Dose | | | Multiple Dose | | |
|---|---|---|---|---|---|---|
| **Type of Surgery** | **Open chole.** | **Lap. Chole.** | **Total** | **Open chole.** | **Lap. Chole.** | **Total** |
| **No. of Patients** | 38 | 9 | 47 | 37 | 10 | 47 |
| **No. of Infections** | 4 | 1 | 5 | 6 | 1 | 7 |

Open Chole: Open Cholecystectomy; Lap. Chole.: Laparoscopic Cholecystectomy

**Table 5:** Duration of Pre Operative Hospital Stay and Number of Infections

| Duration | 0-2 Days | 3-4 Days | 5-6 Days | 7-8 Days | Total |
|---|---|---|---|---|---|
| **Single Dose(47)** | 32 | 12 | 3 | 0 | 47 |
| **No. of Infections** | 2 | 1 | 2 | 0 | 5 |
| **Multiple Dose(47)** | 43 | 4 | 0 | 0 | 47 |
| **No.of Infections** | 7 | 0 | 0 | 0 | 7 |

**Table 6:** Duration of Post Operative Hospital Stay and Number of Infections

| Antibiotic Prophylaxis | 0-2 Days | 3-4 Days | 5-6 Days | 7-8 Days | Total |
|---|---|---|---|---|---|
| **Single Dose (47)** | 42 | 3 | 1 | 1 | 47 |
| **No. of Infections** | 3 | 1 | 0 | 1 | 5 |
| **Multiple Dose (47)** | 22 | 18 | 7 | 0 | 47 |
| **No. of Infections** | 3 | 3 | 1 | 0 | 7 |

**Table 7:** Duration of Overall Hospital Stay And Number of. Infections

| Duration | 0-2 Days | 3-4 Days | 5-6 Days | 7-8 Days | 9-10 Days | Total |
|---|---|---|---|---|---|---|
| **Single Dose(47)** | 1 | 31 | 12 | 2 | 1 | 47 |
| **No. Of Infections** | 0 | 1 | 1 | 2 | 1 | 5 |
| **Multiple Dose (47)** | 0 | 21 | 19 | 7 | 0 | 47 |
| **No. Of Infections** | 0 | 4 | 2 | 1 | 0 | 7 |

## DISCUSSION

The SSI has their implications in term of prolonged hospital stays, increased cost of antibiotics and increased chances of resistant strains of bacteria. The cost of care for patients with surgical site infections is nearly threefold higher than that for surgical patients without the infections during the first eight weeks after hospital discharge.[2]

The gall stone disease is more frequently seen among the female patients in the middle age group. In our study, 91.48% of the patients were females comprising the male: female ratio as 1:10.75. Similar observations were made by Hussain et al[5] and Youseif et al[6] who also observed that gall stone disease was more common in females (88%) as compared to males (12%). More number of SSI were seen by Mahmoud SA et al[7] & Mehmet et al[8] in middle aged female patients (30-50 years) supporting our observations in similar aspect.

In our study, out of 47 people who were administered a single dose of cefuroxime, 5 (10.63%) patients developed infection while the surgical site infection rate was 14.89% in the multiple dose group as 7 patients developed surgical site infection. Overall infection rate was 12.76%. In this study, the rate of wound infection is less in patients with single dose of injection cefuroxime as compared to 5 day conventional antibiotic prophylaxis (p=0.536). Thus, it can be inferred that single dose antibiotic prophylaxis is as good as multiple dose regimen.[9,10]

The optimal time for administration of preoperative doses is within 60 minutes before surgical incision. This is a more-specific time frame than the previously recommended time,

which was "at induction of anaesthesia".[11,12] In our study all the patients in single dose group received the single dose of injection cefuroxime within 60 minutes before the skin incision and 5 (10.63%) patients developed surgical site infection. All the patients in the multiple dose group received the antibiotic prophylaxis outside 60 minutes window and 7 patients developed surgical site infections. 58.33% (7/12) patients developed infection that was given the antibiotic prophylaxis outside the 60 minutes window. The difference was not statistically significant (p=0.910). Steinberg et al[13] & Weber et al[14] also concluded that the SSI rate was low when the prophylactic antibiotic was given within 60 minutes before the skin incision.

Infection rates after laparoscopic cholecystectomy range from 0% to 4% in patients without antimicrobial prophylaxis and from 0% to 7% with prophylaxis. Several studies found that in laparoscopic cholecystectomy SSI rates were significantly lower than those associated with open cholecystectomy. The overall reported rate of postoperative infection in open biliary tract procedures with antimicrobial prophylaxis is 1–19%.[13,15] Also the rate of SSI is higher in the open cholecystectomy as compared to the laparoscopic cholecystectomy. In our study among single dose antibiotic prophylaxis group 10.51 % people developed ssi where as 16.21 % patients suffered an SSI in multiple dose group who underwent open cholecystectomy (p=0.959). One SSI each was noted in laparoscopic cholecystectomy in single as well as multiple dose group. Overall 13.13% infection rate was seen in open cholecystectomy patients (p=0.76) which in accordance with the published data of above mentioned studies. Mehmet et al[8] concluded that antibiotic prophylaxis does not seem to affect the incidence of SSIs and is not necessary for elective LC in low-risk patients. Our study included low risk patients and has also shown a SSI rate of 10.52 % in case of laparoscopic cholecystectomy which is more than the published range.

In our study the incidence of superficial SSI as well as deep SSI was same (4.25%) in case of single dose group whereas in multiple dose group superficial SSI incidence (8.51%) was more. Incidence of deep SSI as well as organ /space SSI was same in both the groups i.e. 4.25% & 2.12% respectively. During this study 50% superficial SSI, 33.33% deep SSI and 16.67% organ space SSI were noted. Health protection agency of U.K. also states that most of the SSI reported affected the superficial layer of the wound (skin or subcutaneous tissues).[16] In terms of major wound infections no statistically significant difference (p=0.58) was found between single-dose and multiple-dose antibiotic regimens in the prophylaxis of biliary tract surgery. Meijer et al[9] supported our study in this aspect.

Among the patient factors responsible for an increased rate of surgical site infection, the pre operative hospital stay is an important factor. According to CDC it can be a surrogate marker for the preoperative co-morbid conditions in a patient.[3] In the present study the pre operative hospital stay was low in multiple dose group, 1.91 days as compared to 2.32 days average stay in single dose group. More number of infections was seen in multiple dose group. The difference was not significant statistically (p=0.87). The rate of infection increased with the duration of preoperative hospital stay in the single dose group but all the infections seen in the multiple dose groups were seen in patients who had a hospital stay of 0-2 days suggesting that there were other factors involved also. Long preoperative hospital stay leads to colonization with antimicrobial resistant microorganisms and affects patients' susceptibility to infection by lowering host resistance or by providing increased opportunity for ultimate bacterial colonization.[17] Anvikar AR[18] and Lilani SP[19] also reported higher rate of SSI in patients with prolonged preoperative hospital stay.

The mean post operative hospital stay in single dose group is less than multiple dose group. So it can be inferred that these infections prolonged their hospital stay. This is in accordance with the internationally reported data which supports the fact that the SSIs increase the duration of hospital stay. In all the other patients the infections were diagnosed after they were discharged from the hospital. Most number of the patients were discharged early in single dose group as compared to multiple dose group thus emphasizing that the infections could have been acquired during the hospital stay. This is in accordance with Holtz & Wenzel[20] who said that 20-70 % of the infections are diagnosed after discharge from the hospital. The average hospital stay of the patients in single dose group who developed infection was 3.2 days ranging from 2-7 days while the average stay of the patients in multiple dose group who developed infection was 2.85 days ranging from 2-5 days (p=0.65). But it can be inferred that the development of a SSI leads to an increase in the length of hospital stay. Hospital stay was more in case of multiple dose groups and more number of infections was seen in the multiple dose group patients. Manian FA[21] showed that the rate of infection increased with the increased hospital stay. In our part of the world the patients sometimes want their sutures to be removed before going home and sometimes they belong to far flung areas where there is scarcity of specialized medical care. They can be

the other factors leading to the prolonged hospital stay in the patients in our study.

In our institution, 469 elective cholecystectomies were done over last one year. Out of them the 402 patients were male and 67 patients were females. In 47 patients single dose antibiotic prophylaxis was employed out of which 5 patients suffered an infection .So effectively 427 patients were given antibiotic over an extended period. If the cost of a single dose of cefuroxime is rupees 150 then for multiple dose group the cost of a 5 days regimen comes out to be rupees 1500. In 427 patients the total cost of treatment was approximately rupees 640500. Whereas this cost for single dose prophylaxis group was roughly rupees 6300 to the hospital. So if the single dose antibiotic prophylaxis is used for elective cholecystectomy the cost of the treatment can be cut to one tenth of the multiple dose regimens. Similarly, Weber et al[14] proposed that single dose of antibiotic was cost effective in the patients undergoing clean contaminated surgery.

## CONCLUSION

In elective cholecystectomy a single dose of intravenous cefuroxime given within 60 minutes doesn't lead to a higher SSI rate as compared to the conventionally given antibiotics which are continued post operatively for a variable length of time. Single dose of antibiotic can certainly decrease the cost of antibiotic therapy to the patient and the institution.

## REFERENCES


1. Ahmed MI. Prevalence of Nosocomial Wound Infection Among Postoperative Patients and Antibiotics Patterns at Teaching Hospital in Sudan. N Am J Med Sci. 2012;4(1):29-34.
2. Perencevich EN, Sands KE, Cosgrove SE, Guadagnoli E, Meara E, Platt R. Health and economic impact of surgical site infections diagnosed after hospital discharge. Emerg Infect Dis. 2003;9(2):196-203.
3. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. The Hospital Infection Control Practices Advisory Committee. Guideline for the prevention of surgical site infection, 1999. Infect Control Hosp Epidemiol 1999;20:247-280.
4. Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. Infect Control Hosp Epidemiol. 1999;20(11):725-730.
5. Hussain M. Quantitative Analysis of Chemical Composition of Gallbladder Stones among Cholecystectomy of Iraqi Patients. American Journal of Research Communication 2013:1(7);26-32.
6. Yousif H. Relationship Between Serum Levels of TSH and Cholesterol with Types of Gallstones. Iraqi postgraduate Medical Journal 2011;10(1):7-12.
7. Mahmoud SA, Khafagy WW, Omar W. antibiotic prophylaxis in elective laparoscopic cholecystectomy: a prospective study. Egyptian Journal of Surgery 2005; 24(3):145-49.
8. Moore EE, Jones TN. Benefits of immediate jejunostomy feeding after major abdominal trauma-a prospective, randomized study. J Trauma1986;26:874-81.
9. Meijer W.S, Schmitz P.I. Prophylactic use of cefuroxime in biliary tract surgery: randomized controlled trial of single versus multiple dose in high-risk patients. Galant Trial Study Group. Br J Surg. 1993;80(7):917–921.
10. Sevin A, Senen D, sevin K, Erdogan B, Orthan E. Antibiotic use in abdominoplasty. J Plast Reconstr Aesthet Surg 2007;60:379–82.
11. Stone HH, Hooper CA, Kolb LD, Geheber CE, Dawkins EJ. Antibiotic prophylaxis in gastric, biliary, and colonic surgery. Ann Surg 1976; 184:443–52.
12. Salkind AR, Rao KC. Antibiotic Prophylaxis to Prevent Surgical Site Infections. Am Fam Physician. 2011;83(5):585-590.
13. Steinberg JP, Braun BI, Hellinger WC, Kusek L, Bozikis MR, Bush AJ. Timing of antimicrobial prophylaxis and the risk of surgical site infection: results from the Trial to Reduce Antimicrobial Prophylaxis Errors. Ann Surg 2009; 250:10-6.
14. Weber WP, Marti WR, Zwahlen M, Misteli H, Rosenthal R, Reck S et al.The timing of surgical antimicrobial prophylaxis. Ann Surg 2008; 247:918-26.
15. Bratzler DW, Hunt DR. The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. Clin Infect Dis. 2006;43(3):322-330.
16. Health Protection Agency. Surveillance of Healthcare Associated Infections Report: 2008. Health Protection Agency. 2008 (available at http://www.hpa.org.uk/web/HPAwebFile/ HPAweb_C/1216193833496.
17. Sachin P. Surgical Site Infections: Incidence And Risk Factors In A Tertiary Care Hospital, Western India. National Journal of Community Medicine 2012;3(2):193-6.
18. Anvikar AR, Deshmukh AB, Karyakarte RP, Damle AS, Patwardhan NS, Malik AK, et al . A one year prospective study of 3,280 surgical wounds. Indian J Med Microbiol 1999;17:129-32.
19. Lilani SP, Jangale N, Chowdhary A, Daver GB. Surgical site infection in clean and clean-contaminated cases. Indian J Med Microbiol 2005; 23:249-52.
20. Holtz TH, Wenzel RP. Post-discharge surveillance for nosocomial wound infection: a brief review and commentary. Am J Infect Control 1992;20(4):206- 13.
21. Manian FA, Meyer L. Surgical site infection rates in patients who undergo elective surgery on the same day as their hospital admission. Infect Control Hosp Epidemiol 1998;19(1):17–22.


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