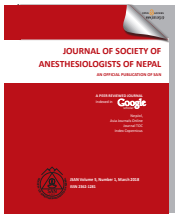

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Original Article

Single dose versus multiple dose antibiotics in laparoscopic cholecystectomy: A prospective comparative single blind study

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Abstract

Introduction: There is a controversy on single dose or multiple doses of prophylactic antibiotics for prevention of surgical site infection during laparoscopic cholecystectomy in a developing country setting. The objective of this study was to compare single versus multiple doses of prophylactic antibiotics in terms of surgical site infection in laparoscopic cholecystectomy patients.

Methods: This was a prospective, comparative, randomized study was conducted in a medical college hospital. Two hundred consecutive patients with symptomatic cholelithiasis planned for routine laparoscopic cholecystectomy were enrolled in the study. Patients were randomly divided in a Single dose (SD) group and multiple dose (MD) group. SD group were given injection ceftriaxone (1gm) before induction of anesthesia and MD group received ceftriaxone (1gm) before induction of anesthesia and continued a total of 3 doses postoperatively for next 24 hours.

Results: A total of 200 patients were studied, of which 100 were in single dose (SD group) and another 100 in multiple dose (MD group). The mean age of patients with symptomatic cholelithiasis was 41.76 ± 13.38 years with minimum of 16 years and maximum of 73 years. Of the total patients, 4 patients in single dose (SD) group and 3 patients in multiple dose (MD) group developed surgical site infection of various severity which was not statistically significant. (p=0.500).

Conclusion: There is no difference in terms of surgical site infection in patients taking either single or multiple doses of antibiotics in laparoscopic cholecystectomy in a medical college setting in Nepal.

Keywords: Antibiotic prophylaxis; laparoscopic cholecystectomy; surgical site infection

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Introduction

Symptomatic cholelithiasis is a common health problem in Nepal and other developing countries. Langenbach performed the first open cholecystectomy in 1892 and Philip Mouret introduced laparoscopic cholecystectomy, which is now considered as a gold standard treatment for symptomatic cholelithiasis.[1]

Surgical site infection (SSI) is one of major problems in any type of surgery. Despite the minimally invasive nature of laparoscopic cholecystectomy, SSI is still prevalent among this group of patients. The use of prophylactic antibiotic has impact in reducing SSI.[2,3] However, excessive use of antibiotics may lead to unnecessary cost, adverse effects of drugs and more importantly emergence of multiple drugs resistant microorganisms. Different studies recommend different antibiotic regimen during laparoscopic cholecystectomy.[4,5] However, most of the studies have been conducted in high income country setting where the higiene of the operating rooms, the laminar air flow system, automatic doors and operating room environment may also contribute to lesser number of SSIs postoperatively but are different from that of a developing country like Nepal.

We designed this study with the aim to compare the single dose versus multiple doses of antibiotics in terms of surgical site infections (SSI) in laparoscopic cholecystectomy patients in a teaching hospital in Nepal.

Methods

This was a prospective, comparative, randomized study, conducted on the patients, diagnosed as symptomatic cholelithiasis and planned for laparoscopic cholecystectomy. Patients admitted through Outpatient Department of General and Minimal Invasive Surgery of Nobel Medical College and Teaching Hospital, Biratnagar, Nepal from June, 2017 to May, 2018, were included in the study after taking ethical clearance from Institutional Review Committee. The diagnosis of cholelithiasis was made on the basis of history, clinical examinations and confirmed by ultrasonography of abdomen and pelvis. The operating rooms where the surgical procedures were performed are regular air conditioned non-modular operation theatres.

Inclusion and exclusion criteria and sample size

All consecutive patients of all age group and both sexes were included in the study. Informed written consent was obtained from all the patients who were enrolled in this study and their age and gender were recorded for demographic comparison.

Patients having choledocholithiasis, cholangitis, biliary pancreatitis, biliary fistulas, patients converted to open cholecystectomy and allergic to the study-drug Ceftriaxone were excluded from the study.

Considering that the overall infectious complication rate in the Single dose antibiotics group would be 6%[6] and that in the multiple dose antibiotics group would be 2%. We designed the trial to detect a 4% difference in the occurrence of surgical site infection between the two groups with a power of 80%. A sample size of 83 was required in each arm. To compensate for possible dropouts, we took a sample of 100 participants in each arm.

We used computer generated random allocation sequence which was stored in sequentially numbered containers and coded. Decoding of the allocated intervention was done only after all the data was collected. A surgical resident took consent from the patients or guardians for participation, generated the random sequence and allocated group distribution.

Interventions

All patients underwent standard four or three ports Hasson's technique Laparoscopic cholecystectomy. The patients were randomly allocated on one of the following groups with 100 patients in each group-

SD group: Patients received intravenous ceftriaxone (1 gram) just before induction of anesthesia.

MD group: Patients received ceftriaxone (1 gram) just before induction of anesthesia and continued twice a day for 24 hours postoperatively (total three doses).

The anesthesia resident administered the study drug in all the patients of both the groups just before induction of anesthesia. The patients allocated to group MD received two more doses of Ceftriaxone administered by ward nurse according to group allocation as directed by the surgical resident. The surgical resident, anesthesia resident and the ward nurse did not participate in the data analysis. The surgeon and all the authors were blinded after assignment to group intervention till complete data was collected.

Postoperative analgesics and antipyretics were standardized in both the groups. All patients were observed till 2nd postoperative day and were discharged, with follow up on 2nd week in Surgical Outpatient Department. During follow up suture removal, wound inspections and collection of histopathological reports of gallbladder was done by the surgeon. Patients were further followed up on 4th weeks of operation.

Primary outcome measure was surgical site infection and was defined as infection occurring within 30 days after the operation involving skin and subcutaneous tissue of the incision and at least one of the following:
1. Purulent drainage with or without laboratory confirmation, from the surgical incision
2. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision
3. At least one of the following signs or symptoms of infection: pain or tenderness, localised swelling, redness, postoperative fever or heat and superficial incision if deliberately opened by surgeon, unless incision is culture-negative
4. Diagnosis of superficial incisional SSI made by a surgeon or attending physician.

These types of wounds were managed with dressing changes, suture removal, wound swab for culture and sensitivity, analgesics, antipyretics and antibiotic treatments as per hospital protocol.

Statistical Analysis

The results of the study were statistically analyzed using SPSS version 22, using chi-square test and independent sample t-test. Results on continuous measurements are presented on mean ± SD (min-max) and results on categorical measurement are presented in numbers (%). A p-value of <0.05 was considered statistically significant.

Results

A total of 207 patients were assessed for eligibility, 7 patients were excluded as 5 declined to participate, 1 patient had choledocholithiasis and one patient was allergic to ceftriaxone. A total of 200 patients were randomized, of which 100 were in single dose (SD group) and another 100 in multiple doses (MD group), received intended treatment and were analyzed. Out of 200 patients, 161(80.5%) were female and 39(19.5%) were male with female to male ratio (4.1:1). The mean age of patients with symptomatic cholelithiasis was 41.76 ± 13.38 years with minimum of 16 years and maximum of 73 years. The highest number of disease was observed in the patients between 30 to 39 years (27%) as shown in Table 1.

Table 1: Distribution of patients in different age groups.

Age Group (Yr)	No. of Patients
11-20	3 (1.5%)
21-30	36 (18%)
31-40	54 (27%)
41-50	47 (23.5%)
51-60	37 (33.5%)
61-70	15 (7.5%)
71-80	8 (4%)
Total	**200**

Out of 200 patients, 100 patients received single dose of ceftriaxone (1gm) at the time of induction of anesthesia (SD group) and next 100 patients received multiple doses of ceftriaxone (1gm) at the time of induction of anesthesia and continued postoperatively twice a day for 24 hours (MD group). The demography of two groups does not show any statistically significant difference (Table 2).

Table 2: Demographic comparison of SD group and MD group

		SD Group n=100	MD Group n=100	p value
Sex	Male	17 (17.0%)	22 (22.0%)	0.476
	Female	83 (83.0%)	78 (78.0%)	
Age (years)		42.21 ± 13.59	41.30 ± 13.21	0.632

Out of 100 patients in SD group, 1 patient (1%) developed fever on first postoperative day which was simply improved with antipyretic drugs. Another 2 patient (2%) had erythema, redness, tenderness around umbilical port at 2nd week follow up, which was improved with suture removal and anti-inflammatory drugs alone. One patient (1%) had wound discharge which was improved with suture removal, drainage of collection and a course of antibiotics. Wound swab was sent for culture and sensitivity which turned out to be sterile. All these patients were followed up to 4th week and were found to be asymptomatic (Table 3).

Table 3: Wound complications in SD group (n=100).

Type of SSI	First postoperative day	Second postoperative day	After 2nd week	After 4th weeks
Fever	1	0	0	0
Port site redness, tenderness	0	0	2	0
Discharge from wound	0	0	1	0
Wound gape	0	0	0	0
Wound abscess	0	0	0	0

Similarly, out of 100 patients in MD group, 2 patients (2%) developed umbilical port site redness and tenderness which was improved with anti-inflammatory drugs at 2nd week follow up. Another one patient developed wound gape, which was improved with daily dressings and a course of antibiotics. Wound healing occurred by secondary intention without need of any suturing by 3rd week (Table 4).

Table 4: Wound complications in MD group (n=100).

Type of SSI	First post-operative day	Second post-operative day	After 2nd week	After 4th weeks
Fever	0	0	0	0
Port site redness, tenderness	0	0	2	0
Discharge from wound	0	0	0	0
Wound gape	0	0	1	0
Wound abscess	0	0	0	0

On further evaluation of wound infection between two groups, 4 patients in single dose (SD) group and 3 patients in multiple doses (MD) group develop infection of various severity as shown by figure 1. There was no statistically significant difference in incidence of wound infection in SD group compared to that of MD group (p=0.500) as shown in Table 5.

Table 5: Comparison of wound infection between two groups using chi-square test.

	Wound infection, n (%)	No wound infection, n (%)	p-value
Single dose (SD group)	4 (4%)	96 (96%)	
Multiple dose (MD	3 (3%)	97 (97%)	0.500

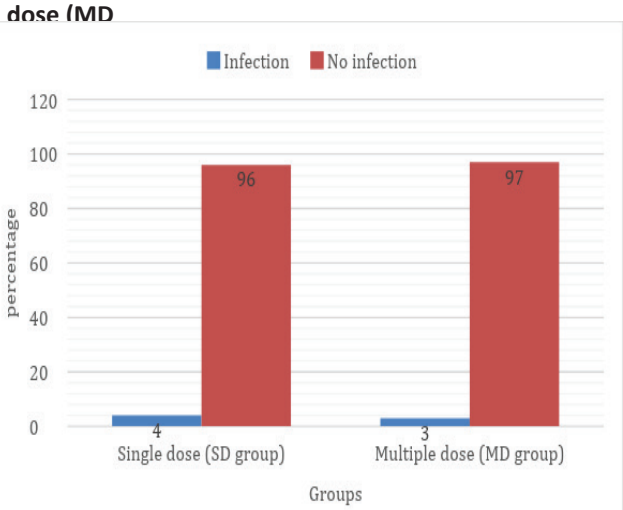

Figure 1: Comparison of wound infection between two groups.

DISCUSSION

Surgical site infection (SSI) is common problem in any surgical procedure. This leads to increase in hospital stay, cost, morbidity and mortality. To reduce SSI, antibiotic prophylaxis has definitive role in clean contaminated and contaminated surgery.[4,5,6] However, the use of antibiotic prophylaxis in clean surgery like laparoscopic cholecystectomy is still questionable. Laparoscopic cholecystectomy has less chance of SSI because there is minimal handling of tissues, less contamination, smaller incisions.[7],[8] Study conducted by Chang WT et al do not recommend the use of prophylactic antibiotics in laparoscopic cholecystectomy.[9] Other study conducted by Sutariya PK et al show single dose of antibiotics is enough preoperatively.[5] A study done by Abro et al concluded that multiple doses of antibiotics should be used instead of single dose.[10] However, most of the studies were conducted in high income countries where the operating room conditions and hygiene level are different. The present study aimed to compare the single dose versus multiple doses of antibiotics in terms of SSI in laparoscopic cholecystectomy patients.

Gall stone disease commonly affects female population compared to male. In the present study, female patients were 161(80.5%) and male patients were 39(19.5%) therefore, female to male ratios was 4.1:1. A study conducted earlier in our institute showed female predominance (82.5%).[11] Gall stones disease generally affects 4th decade of life. In our study age range of patients varied between 16-73 years with maximum patients in the age range between 30-39 years (27%) followed by 40-49 years (23%). Mean age of the patients was (41.76+13.38) years, which coincides with the study conducted in central Nepal and Saudi Arabia.[12,13] Age has been identified as the independent risk factor in open cholecystectomy but has no relation to SSI in laparoscopic cholecystectomy.

Among the 100 patients in SD group, wound infection rate was found to be 4%. One patient (1%) developed fever in first postoperative day, another two patients (2%) had port site redness, tenderness, and another one patient (1%) developed wound discharge. All these patients were managed conservatively with antipyretics, analgesic and wound dressings and all these patients were asymptomatic by 4th week follow up. Whereas in MD group wound infection rate was 3%. Two patients (2%) had port site redness, tenderness and another one had wound gape which was improved with conservative management and became asymptomatic by 4th week follow up. Overall rate of surgical site infections (SSI) in our study is 3.5%. The study conducted by Gaur et al and Koc et al showed that the wound infection rate in laparoscopic cholecystectomy was 2-3% which is comparable with our study.[14,15]

Wound infection rate in SD group is 4% whereas in MD group it was 3% which is statistically insignificant (p=0.5). This signifies that single dose of antibiotics is equally effective

compared to multiple doses of antibiotics in terms of SSI, although some studies support use of multiple doses of antibiotics.[10] However, similar to ours, a study conducted by Meijer et al didn't show any difference in terms of SSI whether single or multiple doses of antibiotics was used.[16] Likewise, Waldvogel and colleagues recommend antibiotic prophylaxis not more than 24 hours.[17]

The strength of this study is its sample size adequately powered to detect surgical site infection. The results of this study may be applicable to other centres in Nepal and developing countries as the settings of interventions and operating room environment are similar. The main limitation of the study is single blind nature and the study is a single centre study.

In conclusion, use of single dose of antibiotic just before induction of anesthesia for laparoscopic cholecystectomy is equally effective as compared to the use of multiple doses of antibiotics in postoperative periods in terms of surgical site infection. However, it would have been more informative if the study was larger and was conducted on patients from multiple centers.

Conflict of interests

All authors have filled the ICMJE conflict of interest form and declare that they have nothing to disclose.

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