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Optimizing ceftriaxone prophylaxis in elective laparoscopic cholecystectomy: single-dose versus multiple-dose antibiotics

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Abstract

Introduction: Prophylactic antibiotics are widely used to reduce the risk of wound infection. However, the necessity of postoperative antibiotic use, its dose and duration remain controversial. This study aimed to compare a single dose of antibiotic against multi doses on wound infection rate in elective laparoscopic cholecystectomy.

Method: A prospective comparative study was conducted at department of surgery in Chitwan Medical College from Sep to Dec 2024. Ethical approval was obtained. Symptomatic cholelithiasis patients undergoing elective laparoscopic cholecystectomy were allocated for single dose (SD) or multiple dosage (MD) groups. First case was selected by lottery and then alternated. Injection 1 gram of ceftriaxone was administered to the SD group at the time of anaesthesia induction, while the MD group got it twice daily for two days. Data on clinico-demographics and wound infection status were recorded in a structured proforma. Frequency, percentage, measure of central tendency and measure of dispersion were calculated. Chi square test/Fischer's exact was used in IBM SPSS for association between SD/MD and wound infection rate. A $p \leq 0.05$ was considered statistically significant.

Result: The study included 126 patients, SD=59 and MD=67. The mean age was 46.68±15.43 years (range: 19–81 years). Wound infections occurred in two patients in each group (SD=3.4%, MD=3.0%), the difference was statistically not significant (p=0.897).

Conclusion: Wound infection following laparoscopic cholecystectomy was low around 3%, and there was no significant difference in the single dose antibiotics versus multiple doses.

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Introduction

Gallstone is one of the most commonly encountered diseases worldwide, with a global prevalence of approximately 6%, showing a higher incidence rate among females and in regions like South America. In Nepal, the incidence ranges between 2.44% to 6.45%.[1,2] Laparoscopic cholecystectomy (LC) was first done on 12 Sep 1985, and has become the gold standard of treatment for gall stone disease.[3–10]

Wound infection is a common problem in surgical practice, though its incidence has declined with technological and medical advancement including perioperative use of prophylactic antibiotics.[11] In laparoscopic procedures the incidence of wound infection is about 0.4%-1.1% which is lesser than open surgery.[12] Indiscriminate antibiotic use can result in needless expenses, adverse drug reaction, and most importantly the development of antibiotic-resistant bacteria. Studies have proposed different antibiotic regimens for LC.[1,12]

Studies done in Nepal on effectiveness of single-dose (SD) and multi-dose (MD) of prophylactic antibiotics in LC fall short to settle the dispute on different regimen, most favouring decreased use of antibiotics.[13,14] The optimal regimen is still debated.[1]

This study aims to compare the effects of SD versus MD antibiotic prophylaxis on the incidence of wound infections following elective LC for symptomatic cholelithiasis. The findings may add to the body of evidence for optimization of antibiotic use and provide necessary insight for further research.

Method

A prospective comparative study was conducted in the Department of Surgery Chitwan Medical College Teaching Hospital, Nepal from Sep 2024 to Dec 2024. Ethical approval was obtained from the CMC Institutional Review Committee (Ref. CMC-IRC/081/082-018).

The study included patients with symptomatic cholelithiasis who underwent elective LC. The study excluded ASA III and IV, and high risk complicated cholelithiasis like biliary pancreatitis, cholangitis, choledocholithiasis, acute calculus cholecystitis, conversion to open cholecystectomy, and those who were lost to follow-up. Written informed consent was obtained from patients or their family members prior to surgery. A structured proforma was used to collect comprehensive patient data, including clinicodemographic, and wound infection.

Patients were categorized into two groups, single dose (SD) which received 1 gm of intravenous Ceftriaxone at the time of anaesthesia induction, and the multiple doses (MD), which received the same dose twice daily for two days.

The sample size was calculated using the formula[15]

$$n = \frac{r+1}{r}\frac{p^*(1-p^*)(Z_\beta + Z_{\frac{\alpha}{2}})^2}{(p_1 - p_2)^2}$$

Where, r=ratio of control to cases=1 for equal number in each group, p*=average proportion exposed=(proportion of complications with single dose antibiotics + proportion of complications with multi dose antibiotics/2, Z_β=standard normal variate for power=0.84 (for 80% power), $Z_{\alpha/2}$=standard normal variate for level of significance=1.96 (for 5% significance level), p1–p2=effect size, p_1=proportion of complications with single dose antibiotics=0.19[16] and p_2=proportion of complications with single dose antibiotics=0.025.[13]

Based on the calculation, the sample size calculated was 56 patients in each group. Considering the potential for attrition, 67 patients were initially enrolled in each group.

Laparoscopic cholecystectomy was carried out as hospital practice, using standard 4-ports and discharged in 1 or 2 days if there are no complications. The umbilical port was used to remove the gall bladder. Wounds were inspected on the second postoperative day before discharge and again during routine follow-up in outpatient department after one week when histopathology reports are usually reviewed as per hospital practice. Port-site wounds were assessed and considered presence of wound infection if redness, swelling/collection, pain, rise in temperature, discharge or gaping preset. We did not follow-up for 30 days (as suggested

by CDC- Centers for Disease Control and Prevention), because most patient in local scenario come accompanied by family members, usually from other town requiring hours of commuting and have to stay in hotels around the hospital. Follow-ups are minimised and done only when necessary. Just to meet guidelines for research, the extended follow-up may not be socially and ethically a good practice. Similarly, we did not investigate for deep surgical site infection routinely. Patients were managed as per hospital practice for wound infection including dressing, pus culture, interventions as required. We did not analyse these data, as our objective was to find out the incidence of wound infection.

The data were entered into the Microsoft excel 2023, statistical analysis was performed by IBM SPSS 23. Central tendency and dispersion of data was assessed. Descriptive statistics (frequency, percentage) were used to summarize the data. Chi-square/Fischer's exact test was used for association of SD/MD and wound infection rate. A p≤0.05 was considered statistically significant.

Result

The study included 126 patients undergoing elective laparoscopic cholecystectomy, randomly assigned to single-dose (SD, n=59) and multiple-dose (MD, n=67) ceftriaxone prophylaxis groups, Figure 1.

The female to male ratio was 0.6:1 and 0.4:1 in SD group and MD group respectively. The gender distribution was not statistically significant (p=0.281). Most of the patients were in the age group of 31-40 years, Table 1.

The overall postoperative wound infection was 3.4% in the SD group and 3.0% in the MD group, with no significant difference between the two groups (p=0.897), Table 2.

There was no adverse drug reactions or complications reported related to antibiotics. The mean hospital stay was 3.02±1.54 days, range 1 day to 9 days. The occurrence of wound infection was similar in both the groups, and were managed as per hospital practice.

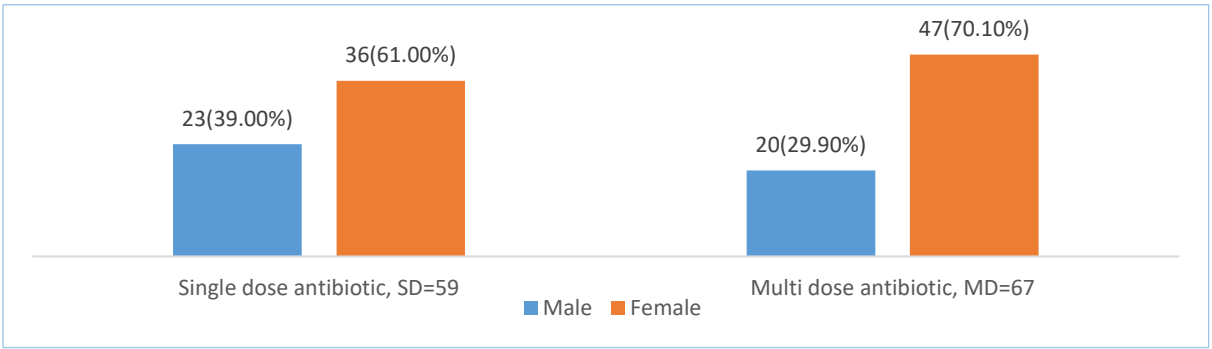

Figure 1. Gender distribution of laparoscopic cholecystectomy (LC) patients receiving SD and MD antibiotic, n=126

Table 1. Age distribution of LC patients receiving SD and MD antibiotics, n=126

Age group years	Wound infection, Yes n(%)	Wound infection, No n(%)
18-30	12(20.3)	3(4.5)
31-40	20(33.9)	20(29.9)
41-50	3(5.1)	14(20.9)
51-60	15(25.4)	13(19.4)
>60	9(15.3)	17(25.3)

Table 2. Wound infections in SD and MD antibiotic group of patients undergoing LC, n=126

Antibiotic use	Wound infection, Yes n(%)	Wound infection, No n(%)	p-value*
Single dose (SD=59)	2(3.4)	57(96.6)	
Multiple dose (MD=67)	2(3)	65(97)	0.897

*Fischer's exact

Discussion

We did not find statistically significant difference (p=0.897) in wound infection rates between the SD and MD groups after elective LC.

In our study, 71.4% of patients were female, which aligns closely with the findings of a studies reporting 83.2% females.[13] Similar female predominance has been documented by most of the studies with female proportions of 91.48%, 82%, and 64.4% respectively.[1,17,18] The female predominance is largely attributed to the influence of oestrogen, which increases cholesterol secretion into bile, thus promoting gallstone formation and subsequent increase of cholecystectomy.[2]

The mean age of patients in our study was 46.68±15.43 years, with the largest proportion (31.7%) in the 31-40 years age group. Gallstone disease typically peaks in middle age. This age distribution is consistent with other studies that report gallstone prevalence in middle to late middle age groups.[19]

The patient's surgical condition and antibiotic use, SD or MD influence the wound infection risk. Various studies[1,14,16,17] have shown that single dose of antibiotic is equally effective to prevent wound infection but some authors recommend that multiple-doses[20] should be used.

The overall wound infection rate in present study was low at 3.3%, a 3.4% in the SD and 3% in the MD antibiotic group. These rates are comparable to similar studies reporting wound infection rates of 3.9% SD vs. 2.5% MD and 4.4% SD vs. 3.3% MD.[1,13] Most studies report similar wound complication of around 2-3%.[22,23] One study reported a much higher wound infection rate of 12.76%, which may reflect differences in surgical technique, patient selection, or perioperative care.[1,17]

The difference in wound infection rates between the SD and MD groups of elective cholecystectomies in our study was statistically not significant (p=0.897), supporting the evidence that single-dose prophylaxis is effective regimens in preventing postoperative wound infections. This finding aligns with other studies that found no significant difference in between SD and MD protocols.[23] One study emphasized the critical importance of antibiotic administration within the first 24 hours post-surgery to prevent infections, even in clean surgical procedures.[24]

The controversies in use of antibiotic in laparoscopic cholecystectomy are a continuing debate since the beginning of LC. Recent studies show a trend towards minimising the use of antibiotics and omit it altogether in selected cases. The controlled trials have shown that the routine use of prophylactic antibiotic in low-risk LC patients (without complicated gall stones like cholangitis, choledocholithiasis, pancreatitis, and requiring conversion) is unnecessary, in local setup as reported in controlled trial conducted more than a decade ago from a teaching hospital in Kathmandu, Nepal.[25] Metanalysis have confirmed the trend of minimising the use of antibiotics.[26]

Minimal use from multiple doses to single dose, from selective low risk patients to acute cholecystitis patients has been expanding the lesser and lesser use of antibiotics in LC. Recent studies including mild to moderate acute cholecystitis has shown that patients do not require antibiotics and they do not have significant increase in postoperative infectious complications compared to those receiving perioperative antibiotics.[27,28] Similar to SD antibiotics in LC, even with the less invasive approach of open cholecystectomy with utilizing mini-incision also do not require MD antibiotic prophylaxis.[29]

Our approach of reducing the use of antibiotic prophylaxis to SD for an elective LC is in line with current global trend of favouring less or no antibiotics to decrease the development of microbial resistance. Single-dose prophylaxis in clean-contaminated surgeries such as LC in present study had similar outcome against unnecessary MD antibiotics. These results have important clinical implications for selective and minimal use of antibiotics in LC, reducing the unnecessary antibiotic exposure in order to prevent antibiotic resistance, decrease costs, and simplify perioperative management without compromising patient safety.

Conclusion

Single-dose preoperative ceftriaxone prophylaxis was equally effective as multiple-doses in preventing wound infection in elective laparoscopic cholecystectomy. The regimen has important implication in clinical practice which may have added benefits of reduced cost, and decreased antibiotic exposure, in line with the global trends favoring less use or no use of antibiotics.

Author contribution

Concept, design: RKM, JNS; Data collection: AS, BKS; Data analysis, interpretation: RKM, JNS, GA; Draft manuscript: RKM, JNS; Manuscript revision: All; Final manuscript: All; and Accountability: All

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Supplementary material
The data and supplementary material that support the findings of this study are available from the corresponding author upon reasonable request.

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