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Randomized clinical assessment of the effect of prophylactic antibiotics in high-risk patients undergoing laparoscopic cholecystectomy

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Abstract
Aim: Prophylactic antibiotics in high-risk patients undergoing laparoscopic cholecystectomy.
Methods: A randomized controlled trial study was conducted in the Department of General Surgery,…….for the period of 1 year. Patient admitted for Laparoscopic cholecystectomy were randomized into two groups A (who did not receive prophylactic antibiotics) and B (those who received antibiotics).
Results: A total of 160 patients were included with Group A and B included 80 and 80 patients, respectively, with similar baseline demographic characteristics and preoperative indications for cholecystectomy. Surgical site infection occurred in six and four patients in the study and control group, respectively. All Surgical site infections were superficial and responded to conservative management only. None of the infected patients required intravenous therapy or hospitalization. Mean duration of hospital stay in patients not having received prophylactic antibiotics (Group A) approached significance (p=0.371) though the range (in days) was the same in both the groups.
Conclusion: Prophylactic antibiotics play no role in the prevention of SSI in patients at high risk, undergoing laparoscopic cholecystectomy. The key to preventing postoperative infection lies in the aseptic minimally invasive operation and the necessary peritoneal lavage and drainage during LC.

Keywords: Laparoscopic cholecystectomy, high risk, antibiotics prophylaxis

Introduction
The average rate of SSIs for LC has been reported in the literature to be between 0.4% and 6.3%, which is lower than rates reported for open cholecystectomy [1-3] Unlike for open cholecystectomy, many investigators have suggested that antimicrobial prophylaxis is probably unnecessary for LC patients because the infection rate for LC is already low, and the use of prophylactic antibiotics does not decrease the rate of wound infections or other postoperative infection complications [1, 4-8]. Also, these recent meta-analyses and systematic reviews have concluded that a prophylactic antibiotic for elective LCs in low-risk patients is not useful, but there were no results in high-risk patients [9].
Despite these studies on the topic, many other surgeons still use and recommend the administration of prophylactic antibiotics for LC in low-risk patients. Generally, preoperative single-dose cefazolin as a prophylactic antibiotic has been recommended and widely used in clean-contaminated surgeries such as cholecystectomy and biliary surgery to reduce SSI [10].

Material and methods
A randomized controlled trial study was conducted in the Department of General Surgery, ……. for the period of 1 year, after taking the approval of the protocol review committee and institutional ethics committee.

Inclusion criteria
- Diagnosed case of cholelithiasis with any high-risk factor
- Age > 18 years

Exclusion criteria
- Pregnant and lactating females.

- Patients requiring antibiotics for any other reason
- Immunocompromised patients
- Evidence of active cholangitis/pancreatitis
- Moribund patients
- A patient who did not consent for surgery
- On table preclusion of laparoscopic surgery

Definitions

High-risk patients – These patients had one or many of the following

1. Age >70 years,
2. Obesity (BMI ≥30)
3. Diabetes mellitus
4. Acute cholecystitis with cholelithiasis with or without its complication (mucocoele/empyema/gangrenous gall bladder).

Surgical site infection (SSI) was classified as superficial surgical site infection, deep surgical site infection and distant site infection.

1. A superficial surgical site infection was defined as erythema and/or purulent discharge from any of the port site, superficial to the fascia.
2. A deep surgical site infection was defined as erythema and/or purulent discharge present deep to the fascia or in the gall bladder fossa
3. A distant site infection was defined as any infection remote to the surgical site.

Methods

Patient admitted for LC from surgical outpatient or emergency were randomized into two groups A and B, on the basis of computer-generated randomization tables. Group A patients received no antibiotics preoperatively. Only oral analgesics, proton pump inhibitors and supportive treatment were advised in usual doses, and these patients were followed up during the entire period of their hospital stay. If antibiotics needed to be administered (on the basis of clinical or laboratory suspicion), it was not withheld, but the patient was then excluded from the study.

Group B patients received a single dose of intravenous antibiotic (first generation Cephalosporin- intravenous Cephazolin 1-2 grams/day) within ≤ 60 minutes prior to the surgery. These patients also received postoperative care, similar to Group A patients.

Culture from the suspected site of infection was to be collected aseptically. The area around the surgical wound was cleaned with 70% ethyl alcohol, and the exudate was collected from the depth of the wound using two sterile cotton swabs, one for Gram stain and another for culture. Utmost care was taken not to touch the surrounding tissues to prevent contamination of swab from endogenous resident flora.

The samples that were collected were sent to the laboratory immediately for processing, to avoid desiccation and to prevent the growth of some species at room temperature that may negate the detection of the true pathogens.

Statistical analysis

Data were recorded in a pre-designed, standardized data collection proforma and later entered in Microsoft Excel 2013 sheet. It was analyzed using the statistical software SPSS version 25.0 (SPSS Inc. Chicago, IL, USA).

Results

A total number of 210 patients fulfilled the inclusion criteria. Of these 22 patients did not consent for participation in the study, and 8 patients were immunocompromised. Hence 180 patients were finally enrolled for the study. However, 14 patients had to be converted to open cholecystectomy, and 6 patients had evidence of gall bladder malignancy. Hence these were also excluded as per the study protocol. Accordingly, 160 patients were finally included in the study.

Group A and B included 80 and 80 patients, respectively. Baseline demographic characteristics (Table 1) and preoperative indications for cholecystectomy (Table 2) were similar in both groups. Intra-operative details were also not statistically different in the two groups. (Table 3). Since our study included patients having one or more preoperative risk factors for the development of SSI, a detailed analysis of risk factor status was also done. There was no statistically significant difference as regards the risk factors in the study and control groups. (Table 4) Surgical site infection occurred in six and four patients in the study and control group, respectively. (Table 5) All SSIs were superficial and responded to conservative management only. None of the infected patients required intravenous therapy or hospitalization. Mean duration of hospital stay in patients not having received prophylactic antibiotics (Group A) the range (in days) was the same in both the groups. All patients developed superficial SSI of the epigastric port (Gall bladder extraction port).

Table 1: Demographic and preoperative details

		Group A N=80	Group B N=80
Age		58 (25-80)	59 (28-80)
Sex Ratio (M:F)		(36:44)	(30:50)
Address	Rural	60	54
	Urban	20	26

Table 2: Indications of cholecystectomy

Indications	Group A N=80	Group B N=80
Chronic cholecystitis with cholelithiasis	25	42
Acute cholecystitis with cholelithiasis ± sequelae (mucocoele/ empyema gall bladder/ gangrene)	37	20
Polyp	4	4
Post pancreatitis	8	7
Post ERCP (Endoscopic Retrograde Cholangio Pancreaticography)	6	7

Table 3: Intra-operative details

		Group A N=80	Group B N=80	P value
Duration of surgery	Difficult dissection (>30 mins for Calots dissection)	18	21	0.462
	Previous upper abdominal surgery	10	6	0.136
Bile spillage		20	23	0.299
Drain insertion		32	30	0.421

Table 4: Numbers of risk factor

Risk factor	Group A N=80	Group B N=80
One	41	43
Two	33	34
Three	4	2
Four	2	1

Table 5: Post-operative outcomes

SSI	Group A N=80	Group B N=80	P value
Superficial	6 (4.8%)	4 (3.2%)	0.268
Deep	0	0	NA
Distant	0	0	NA
Hospital stay (days) mean ± SD	2.02 ± 0.54	2.03 ± 0.57	0.371

Discussion

SSIs are a common performance metric in assessing the quality of health care Centres for Disease Control and Prevention (CDC) recently recommended that only a single dose of preoperative antibiotics should be administered to patients undergoing clean-contaminated procedures based on data from a variety of surgical disciplines. Laparoscopic cholecystectomy is one such procedure, and we wished to see whether a single dose too was mandatory or not. This was done because a routine and indiscriminate use of antibiotics promoted the menace of antibiotic resistance and associated complications [11].

Studies in the past have evaluated the role of prophylactic antibiotics in surgeries of various organ systems [12-14] in various other biliary surgeries [15-18], the role of single versus multiple doses [10] and timing of administration of antibiotics [19-21]. To the best of our knowledge, however, no study which has evaluated the role of prophylactic antibiotics in patients undergoing LC has included all patients with risk factors.

This study includes 160 patients all with high-risk factors in whom 80 patients did not receive any prophylactic antibiotics, and this is in comparison to a recently published study [8] in whom prophylactic antibiotics were not given in only 50 patients, there is no mention about the presence and absence of high-risk factors in these 50 patients.

In our study, the study population randomized to receive or not receive prophylactic antibiotics had similar demographic, preoperative and intraoperative details (as evident from the non-significant p values) suggesting the uniformity in baseline characteristics.

Since SSI developed only in 6 of patients, a multivariate logistic regression analysis (as planned earlier) for determining the effect of each risk factor in the development of SSI, was not carried out).

Incidence of SSI was found to be low in our study in the groups which had received prophylactic antibiotics. Similar results have been seen in other studies as well [22].

In our present study we had bile spillage in twenty-five patients in the study group and twenty-five patients in the control group, these include both, bile spillage during surgery, i.e. iatrogenic and due to primary pathology, for example, gangrenous/ perforated gall bladder. As a routine, we did not perform bile culture because this method does not guarantee the preoperative identification of which patients have bactibilia. Our results are in accordance with the recently published article by Hui TT *et al.* [23] in which no SSI was noticed in gall bladder perforation.

Use of prophylactic antibiotics was recommended in all patients undergoing cholecystectomy [24] or to those over the age of 60 years or with a history of previous attacks of acute cholecystitis [25] in the 20th century. Later, however, several studies have proved that prophylactic antibiotics, not even a single dose [8] decrease the risk of SSI after laparoscopic cholecystectomy [26]. However, none of these studies had all patients with some of the other risk factors.

Mean duration of hospital stay in patients not having received prophylactic antibiotics (Group A) the range of duration of hospital stay (in days) was the same in both the groups. The patient was usually discharged on the next day of surgery. However, in the majority of cases, it was the psyche of the patient that he is ill and requires further hospitalization that leads to a relatively longer duration of stay, instead of surgical reasons. Our results are consistent with the meta-analysis conducted by Choudhary, A *et al.* [27] in terms of hospital stay.

Conclusion

Prophylactic antibiotics play no role in the prevention of SSI in patients at high risk, undergoing laparoscopic cholecystectomy. The key to preventing postoperative infection lies in the asep tic minimally invasive operation and the necessary peritoneal lavage and drainage during LC.

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