ORIGINAL ARTICLE

Use of Antibiotic Prophylaxis in Low-Risk Laparoscopic Cholecystectomy is unnecessary: A Clinical Trial

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ABSTRACT

Background: Laparoscopic cholecystectomy uses smaller incision and trocars that lessen the contamination and exposure of wound, resulting in less infection[1]. However, the antibiotic prophylaxis is still widely practiced, like in our institute, a continuation of the era of open surgery[1-3]. Recent studies reveal no advantage of routine use of antibiotic, and there is growing consensus against it. Besides cost, antibiotic increases emergence of multidrug resistance. Because of the controversies, we conducted this clinical trial.

Methods: This randomized clinical trial, conducted from October 1, 2009 to October 31, 2012 at KVSS Site Hospital Karachi, included 154 patients in prophylactic antibiotic group (GrAP) with cefazolin 1 g IV as per existing practice and 156 in no antibiotic group (GrAPn). Symptomatic laparoscopic cholecystectomy patients of American Society of Anesthesiologist (ASA) 1 and 2 (without diabetes) were included. Patients with complicated gall stones (cholangitis, choledocholithiasis, and pancreatitis) and who required conversion were excluded. Wound was observed during follow-up within 1 week. Data on patient characteristics, use of antibiotic, bile spillage, and postoperative wound infection were entered in predesigned proforma. Microsoft Excel was used to analyze the data.

Results: In total, 310 patients were eligible for analysis, 154 in GrAP and 156 in GrAPn. Both groups were comparable in patient demographic and clinical characteristics such as average age (40.3 vs. 41.6 years) and sex (female 77.6% vs. 78.6%). Overall wound infection occurred in 4.8% (15/310). There was no significant difference in wound infections among the two groups (p = 0.442): GrAP 3.9% and GrAPn 5.8%. There was no mortality in this series.

Conclusion: Routine preoperative antibiotic prophylaxis is not necessary in low-risk symptomatic gallstone patients undergoing laparoscopic cholecystectomy.

Keywords: Antibiotic prophylaxis,laparoscopic cholecystectomy, surgical site infection

INTRODUCTION

Laparoscopic cholecystectomy (LC) has now come of age as a safe surgery for symptomatic cholelithiasis. Regarding the use of antibiotic prophylaxis (AP) in LC, despite the controversies, there is a growing consensus in support of not using AP in uncomplicated cases[1,2,3,4,5]. However, clinicians do not give up the traditional practice easily despite the fact that recent meta-analysis and reviews support this view.

Preoperative single-dose cefazolin as an AP has been recommended (by the Centers for Disease Control and Prevention—CDC) and widely used in clean-contaminated surgery such as cholecystectomy and biliary surgery to reduce surgical site infection (SSI)[6,7.]

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The benefit of LC as a minimally invasive surgery has been recognized for its faster recovery, but the use of AP has remained similar to that of the era of open cholecystectomy. This needs re-evaluation because the role of AP to prevent SSIs is controversial in LC due to low risk of SSI. In LC, the incision is smaller and manipulation is done through trocars that lessen the contamination and exposure of wound, unlike in open surgery[8,9,10,11,12,13,14,15,16].

Unnecessary use of antibiotic adds to the cost and increases emergence of multidrug resistance. Because of the controversies on routine use of AP in LC, we conducted this prospective trial on the necessity of our existing practice of using single-dose cefazolin as AP in LC

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PATIENTS AND METHODS

This randomized clinical trial was carried out from October 1, 2009 to September 31, 2012 at KVSS SITE Hospital, a university teaching hospital with optimum operating, anesthetic, and recovery facilities, with the aim of including 150 patients in

each group. Patients were randomized into two groups by lottery. Odd-numbered[1,4,6]. (1 and subsequent[3,5], patients received antibiotic prophylaxis (GrAP), whereas even numbered (2 and subsequent did not receive antibiotic prophylaxis (GrAPn). Operation-room nurses administered antibiotics to the odd-numbered patients.

Symptomatic patients scheduled for LC of ASA 1 and 2 (without diabetes) who consented for the study were included. Patients with complicated gall stones (cholangitis, choledocholithiasis, and pancreatitis) and those who required conversion to open cholecystectomy were excluded. Acute cholecystitis with high leukocyte count (>11,000) and fever (>100°F) prior to surgery were not included in the study. Patients who were found to have suppurative cholecystitis, empyema, or gangrenous gallbladder during surgery were also excluded. However, patients with acute biliary attack of right upper quadrant pain admitted through emergency department were included. The study was approved from the hospital authority. All LCs were performed under general anesthesia with endotracheal intubation. Patients were monitored postoperatively as per our existing practice.

For postoperative analgesia, morphine 4–6 mg (0.1 mg/kg) and Diclofenac Sodium 75 mg were administered intramuscularly every 6 hour as required, together with oral paracetamol 500 mg and ibuprofen 400 mg. Oral feeding was started after 4 hours of surgery. Drip was stopped 6 hours after surgery, with cannula being locked *in situ*. Patients were discharged on 1st postoperative day (if vitals were stable with no features of peritonitis and if patients could tolerate oral feeding). They were advised to follow up in surgical referral clinic within a week. Status of wound (normal, inflamed, or pus) was recorded and managed accordingly with ciprofloxacin 500 mg twice daily for inflammation, plus gaping/dressing of wound in case of pus.

Patient demographics and clinical characteristics, including gall bladder perforation and bile/stones spillage during surgery, were recorded in a predesigned proforma. Microsoft Excel and SPSS were used to analyze the data.

RESULTS

During the study period, a total of 328 LC patients were enrolled out of which 18 were excluded because of incomplete data. Among the remaining 310 patients eligible for analysis, 154 were in GrAP and 156 in GrAPn. Both groups were comparable in patient demographic and clinical characteristics (Table 1).

Inadvertently, perforation and spillage of bile occurred in 96 cases of which 25 also had spillage of stones. Spilled stones were picked up and irrigation with normal saline was performed until the aspirate was clear.

The overall SSI occurred in 4.8% (15/310) of patients. Six SSI out of 154 (3.9%) occurred in GrAP and nine out of 156 (5.8%) in GrAPn. This slightly higher incidence of SSI in GrAPn was not significant (chi-square test, $p>0.05$ or $p=0.442$; Table 2). There was no bile duct injury or mortality in this series. Average hospital stay after surgery was 1.27 (range 1–3) days in GrAP and 1.32 (range 1–3) days in GrAPn.

Table 1: Findings in laparoscopic cholecystectomy patients (*n* = 310), GrAP and GrAPn.

Laparoscopic cholecystectomy patients	**GrAP*n*%**		**GrAPn*n*%**	
Number of patients	**154**		**156**	
Age (y)	40.3	(13–76)	41.6	(10–76)
Female	121	78.6	121	77.6
Male	33	21.4	35	22.4
Bile spillage	52	33.8	46	29.5
Acute biliary attack[a]	11[b]	7.1	20[b]	12.8
SSI (stitch abscess, erythema, discharge)	6	3.9	9	5.8

GrAP=antibiotic prophylaxis group; GrAPn=no antibiotic prophylaxis group; SSI=surgical site infection. A Without leucocytosis, fever, or findings of suppurative cholecystitis, empyema, or gangrenous gallbladder during surgery. B Two out of 11 and four out of 20 also had bile leak.

Table 2: Wound infection among two groups of LC patients with and without prophylactic antibiotic had no significant difference (chi-square test, $p>0.05$ or $p=0.442$).

LC patients	**Wound infection *n*%**		**No wound infection *n*%**	
GrAP, *n*=154	6[a]	3.9	149	96.1
GrAPn, *n*=156	9[a]	5.8	147	94.2
Total, *n*=310	15	4.8	295	95.2

GrAP=antibiotic prophylaxis group; GrAPn=no antibiotic prophylaxis group; LC=laparoscopic cholecystectomy. None of these patients were from the subgroup of acute cases

DISCUSSION

Protocol to AP at our institutions has continued ever since the era prior to the introduction of minimal invasive LC two decades ago. Like many other institutions in and out of the country, all cholecystectomy patients at our hospital routinely receive AP (cefazolin 1 g IV) prior to surgery. In the present study, the overall SSI was 4.8%. The SSI was 3.9% in GrAP and 5.8% in GrAPn. The slightly higher occurrence of wound infection in GrAPn was statistically not significant (chi-square test, $p > 0.05$ or $p = 0.442$). Our findings are comparable with reported studies[1,2,3,5,8,9].

Iatrogenic gallbladder perforation in LC occurs in 2–25% of cases[2,4,17,19]. In the present study, we had higher incidence of bile leakage spillage (30.9%, 96/310). Possible cause could be involvement of acute cases (10%) and different levels of operating surgeons, from lecturer to professors. Findings of this study does not support the general perception that bile leak increases the SSI. Out of 45 bile spillage in GrAPn (156 LC), there were only five SSIs out of the nine that had spill during surgery. Similarly in GrAP (154 LC), there were 50 bile spills, but none of the six SSIs had any history of bile spill. Other studies have reported similar findings[8,17,20].

We did not include body mass index (BMI) as a possible variable to influence wound infection in open surgery, because BMI is not considered a risk factor in minimal invasive LC with small incision. In case of LC, studies have not found differences in operative time, length of stay, or complications between normal-weight and overweight or obese patients[21,22,23]. Moreover, BMI of patients we see in our local society seldom exceeds 30.

In this study, we included patients who were admitted from emergency department with acute biliary pain (without the features of “acute infection” such as high leucocyte count and fever, and findings of empyema, gangrenous or suppurativecholecystitis-thickened and edematous “hot” looking gallbladder during surgery).

Subgroup analysis revealed that 11 acute cases (two also had bile spill during surgery) in GrAP and 20 (with four bile spill) in GrAPn who had LC during the admission did not develop SSIs. Study with larger sample size may be required to generalize our findings that patients with acute attack (but without features of suppurativecholecystitis, empyema, and gangrenous gallbladder) do not benefit from routine AP to prevent SSIs.

There was no difference in average hospital stay after surgery, with 1.27 (range 1–3) days in GrAP and 1.32 (range 1–3) days in GrAPn. Our practice is to discharge patients on the 1st postoperative day following LC unless their condition is complicated (example: unstable vitals or peritonitis due to bile leak) or they are not willing to go home (due to transportation problem when living far from the hospital). In this study, we had no bile leak or duct injury. Also, because of transportation problem we cater service to patients from all over the country and even from within the town, if required. This is the reason why some of our patients who could be discharged medically stayed 1–2 days more after surgery.

This study has some limitations. We did not include patients with “acute cholecystitis” who had high leukocyte count, fever on admission, or findings of suppurativecholecystitis, empyema, or gangrenous gallbladder during surgery. Thus, our findings cannot be generalized to all patients who undergo surgery for acute cholecystitis because they are already on antibiotic when admitted from emergency department. This will require separate study with different sorts of protocols. At our institute, we perform “emergency” cholecystectomy for patients admitted within a week of attack, on any of the four scheduled operation days. Otherwise, they are advised for surgery after 6 weeks or more. We consider “emergency surgery” out of normal operating schedule when there is a complication such as peritonitis due to gangrenous or gallbladder perforation.

Risk of SSI in LC is low and does not seem to be reduced by the routine use of AP in uncomplicated cases, as we found in this study. Based on recent published evidences and after the completion of our own study, we have now adopted the policy of not administering routine AP in uncomplicated cases of LC. Most of the published data come from developed countries that may have different patient and social structures. We hope that being conducted in a local scenario this study will help other institutions in Pakistan as well as in other developing countries with similar socioeconomic condition to benefit from its findings.

CONCLUSIONS

Already low risk of wound infection following LC was not significantly reduced further with the routine use of preoperative AP in uncomplicated patients with symptomatic cholelithiasis.

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