

# The Role of Prophylactic Antibiotics in Elective Laparoscopic Cholecystectomy

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## ABSTRACT

**Background and Objectives:** Elective laparoscopic cholecystectomy has a low risk for infectious complications, but many surgeons still use prophylactic antibiotics. The aim of this prospective study was to investigate the necessity and test the efficacy of prophylactic antibiotics on postoperative infection complications in low-risk patients undergoing laparoscopic cholecystectomy.

**Methods:** Low-risk patients were randomly placed into 2 groups: 68 patients (group 1) received cefazolin 1g intravenously after induction of anesthesia, and 76 patients (group 2) were not given prophylactic antibiotics. In both groups, septic complications were recorded and compared.

**Results:** Positive bile culture and gallbladder rupture did not significantly increase the rate of surgical site infections. In group 1, there were 3 (4.41%) cases of wound infection, 3 (4.41%) cases of pulmonary infections, and 1 (1.47%) case of urinary tract infection. In group 2, there were 2 (2.63%) cases of wound infection, 2 (2.63%) case of pulmonary infections, and 3 (3.95%) cases of urinary tract infection. No significant difference existed in the complication rates.

**Conclusions:** Based on our data, the use of prophylactic antibiotics does not decrease the rate of postoperative infection complications and surgical-site infections and is not necessary in low-risk patients undergoing laparoscopic cholecystectomy.

**Key Words:** Laparoscopic cholecystectomy, Surgical site infection, Prophylactic antibiotics, Endobag extraction.

## INTRODUCTION

Surgical site infections (SSIs), a significant postoperative complication, can lead to considerable patient morbidity and mortality.<sup>1</sup> Preventing postoperative infection is an essential factor in improving the results of surgical procedures. One approach to preventing infection is the administration of prophylactic antibiotics. The benefits of preoperative antibiotics, which reduce bacterial contamination during clean-contaminated operations such as cholecystectomy and contaminated operations, are well known.<sup>1-3</sup>

At present, laparoscopic cholecystectomy (LC) is the standard treatment for symptomatic cholelithiasis. The incidence of infectious complications after LC is significantly lower compared with infections with open cholecystectomy.<sup>4,5</sup> The use of prophylactic antibiotics as a means of preventing SSIs is still controversial in elective LC, which has a low risk for infectious complications. Many authors believe that antibiotic prophylaxis may not be necessary in low-risk patients undergoing elective LC.<sup>6-10</sup> On the contrary, many other surgeons still use and recommend the administration of prophylactic antibiotics.<sup>11-15</sup> McGuckin et al<sup>16</sup> documented in their chart review that 79% of patients who had undergone LC were given prophylactic antibiotics preoperatively.

Because of its broad-spectrum antimicrobial effect, low toxicity, and low cost, the single-dose use of cefazolin has been recommended for patients undergoing open cholecystectomy and other biliary surgery,<sup>2,17</sup> and it was recommended by the United States Centers for Disease Control and Prevention as the general principle for prevention of postoperative surgical site infection (SSI) in open cholecystectomy.<sup>3,18</sup>

Because controversy still surrounds the routine use of prophylactic antibiotics in elective LC, this prospective study was conducted according to the United States Centers for Disease Control and Prevention guidelines with the aim of investigating the necessity and testing the efficacy of single-dose cefazolin as a prophylactic antibiotic to prevent postoperative infection complications in low-risk patients undergoing LC.

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## MATERIALS AND METHODS

A double-blind, prospective, randomized, controlled study comparing the prophylactic use of cefazolin (Group 1) vs placebo (group 2) was performed between January 1, 2005 and December 31, 2007 in our clinic. In all, 343 LCs were performed in this period. Following Institutional Research Ethics Committee approval of the protocol, 150 patients undergoing elective laparoscopic cholecystectomy were selected as suitable for the study protocol. All patients participating in the study gave informed written consent. Exclusion criteria were patients older than 60 years; antibiotic intake in the 7 days prior to surgery; acute cholecystitis in the 6 months prior to the procedure; evidence of cholangitis and/or obstructive jaundice and biliary pancreatitis; regular corticosteroid therapy; pregnancy or lactation; previous biliary tract surgery or previous endoscopic retrograde cholangiopancreatography; presence of American Society of Anesthesiologists classification (ASA) higher than score II; evidence of diabetes mellitus; body mass index higher than 30; and conversion to open cholecystectomy.

Cefazolin (1g) or normal saline was administered intravenously by the anesthesiologist during induction of anesthesia. One of 2 packages containing either cefazolin or placebo was chosen randomly by the anesthesiologist for each patient. The package was opened by the anesthesiologist, and the type of solution administered (*cefazolin or placebo*) was recorded. The medical staff and the patient were unaware of the content of the solution. After induction of anesthesia, the skin was disinfected with a 10% solution of povidone-iodine. LC was performed in all patients by using a 4-trocar technique. A 10-mm trocar was placed with the open technique using an infraumbilical incision. The other 3 trocars were placed under direct vision. A 10-mm trocar was placed in the epigastrium, a 5-mm trocar on the midclavicular line, and a 5-mm trocar in the right flank in line with the gallbladder fundus. If gallbladder rupture and spill of bile or stones was encountered, spilled stones were retrieved whenever possible, and local peritoneal lavage with 1000cc saline was performed. The gallbladder was removed through the umbilical port, always with the use of an endobag that was prepared using a sterile glove without talc. A drain was never placed. A sample of bile was removed by suction with a sterile syringe from the gallbladder immediately after its removal and sent to the microbiology laboratory for bacterial detection.

Antithrombotic prophylaxis was not administered, and a vesical catheter was not inserted. A nasogastric tube was

positioned during the induction of anesthesia and removed at the end of surgery. The postoperative course was monitored, and any incidents, such as fever, infection of the trocar site, or intraabdominal collection of pus, were recorded. After discharge from the hospital, the patients underwent weekly clinical and laboratory postoperative monitoring for SSI for a 30-day period.

The following data were collected for each patient: age, sex, body weight, ASA classification, blood biochemical data, times of antibiotic administration, time of skin incision, gallbladder rupture, bile and/or spillage, positive bile culture, type of fascia and skin closure, duration of surgery, conversion to open cholecystectomy, bile and wound culture results, length of hospital stay, and number of septic complications. Postoperative superficial or deep incisional soft tissue SSI and intraabdominal abscess (organ/space SSI) were defined according to published criteria.<sup>1</sup> If local signs of inflammation or a pus collection were present, bacteriological swabs were taken from the wound site.

Statistical analyses were performed using chi-square test, Fisher's exact test, and Mann-Whitney U-Test. All analyses were conducted using SPSS 10 software (SPSS, Inc., Chicago, IL, USA) with a P-value <0.05 considered as significant.

## RESULTS

Six patients (4 patients from group 1 and 2 patients from group 2) who were converted to open cholecystectomies were excluded from the original groups. Groups 1 and 2 included 68 and 76 patients, respectively. The characteristics of the groups and number of infectious complications are presented in **Table 1**. No significant differences existed between the 2 groups regarding sex, age, body weight, ASA score, conversion to open cholecystectomy, duration of surgery, number of intraoperative gallbladder perforations and spill of bile or stones, number of positive bile cultures, mean postoperative hospital stay, or number of infectious complications. Group 1 had 3 (4.41%) superficial SSIs in the umbilical port site, 3 (4.41%) pulmonary infections, and 1 (1.47%) urinary tract infections, for an overall infection rate of 10.29%. Group 2 had 2 (2.63%) superficial SSIs in the umbilical port site, 2 (2.63%) pulmonary infections, and 3 (3.95%) urinary tract infections, for an overall infection rate of 9.21%. There was no significant association between intraoperative gallbladder rupture or positive bile culture and SSI. The rate of gallbladder rupture in groups 1 and 2 were 13.2% and 15.79%, respectively. SSI occurred in 1 of 21 patients who had a

**Table 1.**

Characteristics of Patients and Infectious Complications\*

Characteristics	Group 1 n = 68	Group 2 n = 76
Sex (M/F)	10/58	12/64
Mean age (y)	44.6±23.4	42.5±21.6
Body weight (kg)	73.3±7.61	74.1±7.73
ASA score (I/II)	58/10	62/14
Conversion n (%)	4 (5.88)	2 (2.63)
Infected bile n (%)	9 (13.2)	13 (17.1)
Bile or gallstone spillage	9 (13.2)	12 (15.79)
Duration of surgery (min)	77±34.2	85.1±32.2
Length of hospital stay (d)	1.117±0.324	1.5118±0.325
SSI (superficial) n (%)	3 (4.41)	2 (2.63)
Urinary tract infection	1	3
Pulmonary infection	3	2

\*P values not significant.

gallbladder rupture and in 4 of 123 patients without rupture ( $P>0.05$ ). The positive culture rates of bile in patients in groups 1 and 2 were 13.2% and 17.1%, respectively, and the difference was not significant. The most commonly isolated microorganisms are summarized in **Table 2**. SSI occurred in 1 of 22 patients who had a positive bile culture and in 4 of 122 patients who had a negative bile culture ( $P>0.05$ ). Wound culture was negative in 2 of 4 patients who had negative bile culture and in the 1 patient who had a positive bile culture. In the other 2 of 4 patients who had a negative bile culture, coagulase-negative *Staphylococcus spp.* and *Staphylococcus aureus* were isolated on pus culture from the wounds. SSI was treated in all patients by pus drainage.

## DISCUSSION

The average rate of SSIs for LC has been reported in the literature to be between 0.4% and 6.3%,<sup>6-8,10,13,16,19</sup> which is lower than rates reported for open cholecystectomy.<sup>4,5</sup> Our data show that the incidence of SSI in patients was 3.47% for the total study group, 4.41% for group 1, and 2.63% for group 2, and in agreement with previous studies, there was no significant difference in infection rate between the groups. All SSIs were superficial SSIs and minor complications.

Although antibiotic prophylaxis is considered standard protocol in open cholecystectomy as a means of reducing the incidence of infectious complications, its use is still debated

**Table 2.**

Microorganisms Isolated From Gallbladder Bile

Microorganism	Group 1 (n = 68)	Group 2 (n = 76)
<i>Escherichia coli</i>	4	6
<i>Enterococcus species</i>	3	3
<i>Klebsiella species</i>	2	2
<i>Pseudomonas aeruginosa</i>	1	2
<i>Staphylococcus species</i>	0	1
<i>Enterobacter aerogenes</i>	0	1
Monobacterial	8	11
Mixed flora	1	2
Total bile culture +	9	13

in LC. Lippert and Gastinger<sup>11</sup> performed a prospective population-based multicenter study to evaluate antimicrobial prophylaxis in laparoscopic and conventional cholecystectomy. They recommend that both laparoscopic and conventional open cholecystectomy be performed with adequate perioperative antimicrobial prophylaxis because patients receiving prophylaxis fared significantly better than those with no prophylaxis in terms of the rate of postoperative infections, other complications, reoperation, and mortality. Similarly, several other studies conclude that the use of prophylactic antibiotics in LC leads to a significant decrease in infectious complications.<sup>12-15</sup> Conversely, many prospective studies have suggested that antibiotic prophylaxis is probably not required in elective LC, because the infection rate of LC is already low and the use of prophylactic antibiotics does not decrease the incidence of SSIs and other postoperative infection complications.<sup>6-10</sup> Goldfaden and Birkmeyer<sup>20</sup> reviewed the perioperative treatment of patients with laparoscopic interventions in 98 randomized studies on antibiotic prophylaxis since 1990. They stated that routine antibiotic use in LC is likely unnecessary for low-risk patients. Catarci et al<sup>19</sup> recommended in their review that a multicenter prospective randomized controlled clinical trial be designed to find a definitive answer to the question of routine antibiotic prophylaxis in LC, because there are no randomized trials with a sufficient number of cases to avoid a type II error. The theoretical number of patients necessary for such a trial was estimated to include more than 3500 patients.<sup>19</sup>

The positive bile culture rate in patients with gallbladder stones has ranged between 10% and 42.5% in previous studies.<sup>6,7,9,12-14</sup> Perforation during gallbladder surgery is attributed to traction, grasping, dissection, and removal of

the gallbladder and occurs in 11% to 35% of LCs.<sup>6,9,12,15</sup> The effect of positive bacteria culture and bile or stone spilling due to perioperative gallbladder perforation on the occurrence of SSI infections is still controversial. Shindholimath et al<sup>13</sup> found that bactibilia was the most important predictor of wound infection in low-risk patients undergoing elective LC. They recommended prophylactic antibiotics to reduce the incidence of wound infection because it might not be possible to determine which patients have bactibilia by routine investigation. Uchiyama et al<sup>12</sup> reported that preoperative prophylaxis with 0.5g sulbactam and 0.5g cefoperazone significantly reduces the positive bile culture, resulting in a significant reduction in complications induced by postoperative infections. However, Dervisoglou et al<sup>14</sup> stated that both positive bile culture and intraoperative gallbladder rupture were strongly associated with development of SSI. Additionally, they determined that SSI was caused by exactly the same pathogens found in intraoperative cultures. In our study, we detected that the overall rate of SSI did not correlate with the presence of bacteria in the bile or gallbladder rupture. Many other studies have also indicated that SSIs are not related to bile culture, rupture of the gallbladder, or spillage of gallbladder stones or bile.<sup>4,6,7,9,10</sup>

On the other hand, there was no relationship between the perioperative organisms isolated from the bile and the subsequent SSI in our study or in other studies.<sup>6,9,21</sup> Tocchi et al<sup>9</sup> in their study identified different microorganisms in pus culture in 10/11 bile culture positive patients which had septic complications. However, Harling et al<sup>21</sup> detected that all organisms isolated from the wound sites of patients who developed SSIs were skin commensals. They did not find a significant difference in rate of SSI between prophylactic antibiotic usage and mechanical isolation of the gallbladder with endobag during extraction from the abdomen. Hamzaoglu et al<sup>22</sup> also reported that the umbilical flora and the bile were not the source of the SSIs after laparoscopic surgery. Also in our study, possibly commensal coagulase-negative *Staphylococcus spp* were isolated from 1 of 2 patients with negative bile culture, and *Staphylococcus aureus* was isolated from the other patient in the pus culture. The wound culture was negative in the other 2 patients with negative and 1 patient with positive bile cultures. We believe that mechanical isolation of the gallbladder from the umbilical wound with routine endobag use in all patients while extracting the gallbladder from the abdomen and local peritoneal irrigation in the presence of gallbladder perforation is effective in preventing contamination with possibly infected bile. The prep-

aration of an endobag from gloves without talc is an easily prepared, effective, and cost-effective method that we routinely use. In our study, despite prevention of contamination with the endobag of the umbilical port area, the fact that all SSI infections occurred at the umbilical port area leads us to believe that entering with the first port open procedure and extracting the gallbladder from the umbilical port leads to more tissue trauma than that sustained in the other wounds at the port entrances.

## CONCLUSION

Based on our data, perioperative gallbladder perforation and possible positive bile culture do not increase SSI rates. Local irrigation in the case of perforation and the mechanical isolation of the gallbladder while extracting it from the abdomen with an endobag in the case of bactobilia seem to be adequate to prevent contamination. Antibiotic prophylaxis does not seem to affect the incidence of SSIs and is not necessary for elective LC in low-risk patients.

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