



A prospective randomized study of prophylactic antibiotics in elective laparoscopic cholecystectomy

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Abstract

Background: Elective laparoscopic cholecystectomy (LC) has a low risk for infective complications, but many surgeons still use prophylactic antibiotics. The use of prophylactic antibiotics for LC is inconsistent and varies widely among surgeons.

Methods: We performed a prospective double-blind randomized study of prophylactic antibiotics in elective LC. Antibiotics were given first before the operation and then again 24 h afterward. Group A ($n = 49$) received 2 g of cefotaxime; group B ($n = 43$) received 10 ml of isotonic sodium chloride solution. A sample of bile was withdrawn by direct gallbladder puncture for anaerobic and aerobic cultures. Age, sex, weight, duration of surgery (DOS), presence of diabetes mellitus, American Society of Anesthesiologists (ASA) classification, gallbladder rupture, bile and/or stone spillage, gallbladder histological findings, findings from bile cultures positive for bacteria, episodes of colic within 30 days before surgery, length of stay (LOS), and number of septic complications were recorded for both groups.

Results: There was no differences between the two groups in terms of sex, weight, DOS, ASA score, gallbladder rupture, bile and/or stone spillage, gallbladder histological findings, findings from bile cultures positive for bacteria, or LOS. One infection occurred in the antibiotic prophylaxis group (2.04%); in the patients not receiving antibiotics, there was one other infection (2.32%). There was no statistical difference between the two groups in infective complications.

Conclusion: In patients undergoing elective LC, antibiotic prophylaxis is justified only in high-risk patients. In all other patients, antibiotic prophylaxis does not seem to affect the incidence of postoperative infective complications. In low-risk patients, eliminating the unnecessary use of prophylactic antibiotics would result in a

cost reduction; moreover, it would lower the risk of adverse reaction and reduce microbial resistance.

Key words: Cholecystectomy — Laparoscopy — Prophylactic antibiotics

Although elective laparoscopic cholecystectomy (LC) has a low risk for infective complications, many surgeons still use prophylactic antibiotics. Moreover, the use of prophylactic antibiotics for LC is inconsistent and varies widely among surgeons.

Antimicrobial prophylaxis for various clean or contaminated surgical procedures has become the standard of practice to reduce the risk of postoperative infection. However, studies have shown that prophylactic antibiotics are not generally indicated for clean operations [1]. The incidence of infective complications after LC is usually low, and it is significantly lower compared to open cholecystectomy. Since LC is associated with smaller wounds and minimal tissue damage, this could help to explain the lower risk of infective complications [8].

The aim of this study was to determine whether prophylactic antibiotic treatment in elective LC further decreases the already low infection rate associated with this procedure.

Patients and methods

All patients undergoing elective LC at the Fifth Department of Surgery, Ankara Numune Teaching and Research Hospital, Ankara, Turkey, from 1 February 2001 to 1 March 2002 were considered for the protocol. Ninety-two patients undergoing elective LC were selected for a double-blind randomized prospective study. After the patients were confirmed for the study, they were randomized into two 105 groups, A and B. Antibiotics were given before the operation and again 24 h postoperatively. Group A received 2 g of cefotaxime sodium diluted in 100 ml isotonic sodium chloride solution; group B received 10 ml of isotonic sodium chloride solution in 100 ml of saline. Both the surgical team and the patients were blinded to the groups.

All of the patients underwent conventional LC using four trocar sites. The skin was prepared with 10% povidone-iodine solution. The

Table 1. Preoperative data and general outcomes

Characteristic	Group A (n = 49)	Group B (n = 43)
Age, yr	50.1 ± 8.2	47.5 ± 7.9
Sex, M/F	18/31	15/28
Weight, kg	74.3 ± 6.2	71.8 ± 6.1
ASA score		
1	20	17
2	26	24
3	3	2
DOS, min	72.4 ± 20.1	70.1 ± 19.8
Gallbladder rupture	8 (16.3%)	6 (13.9%)
Bile spillage	10 (20.4%)	8 (18.6%)
Stone spillage	3 (6.1%)	3 (6.9%)
LOS, d	4.8 ± 0.9	5 ± 0.9
Diabetes mellitus	7 (14.2%)	5 (11.6%)
Infected bile	5 (10.2%)	5 (11.6%)

ASA, American Society of Anesthesiologists; DOS, duration of surgery; LOS, length of stay

Data given as mean ± SD or number of patients

gallbladder was removed through the operating port, with or without the use of a bag. The umbilical incision was closed with a 2-0 nonabsorbable monofilament suture; a 3-0 monofilament suture was used for the other incisions. At the beginning of the operation, a sample of bile was withdrawn by direct gallbladder puncture for anaerobic and aerobic cultures. In addition, the following data were collected for each patient: age, sex, weight, duration of surgery (DOS), presence of diabetes mellitus, American Society of Anesthesiologists (ASA) score, gallbladder rupture, bile and/or stone spillage, gallbladder histological findings, findings from bile culture positive for bacteria, episodes of colic within 30 days prior to surgery, length of stay (LOS), and number of septic complications.

The postoperative course was monitored, and any incidents such as fever, infection of the trocar site, or intraabdominal collection of pus were recorded. All patients were examined by an attending surgeon 7–10 days after the operation and followed up for 30 days. The review included a structured interview and a clinical examination.

In brief, low-risk patients were defined as those without past or present objective evidence of biliary obstruction or recent severe acute infection. Specifically, they were adult patients with objective evidence of low-grade acute or chronic cholecystitis and symptoms compatible with that diagnosis that could not be eliminated by any of the following exclusion criteria: (a) β-lactam or cephalosporin allergy, sensitivity, or anaphylaxis; (b) the receipt of antibiotics within 7 days of the planned procedure; (c) a temperature > 38°C; (d) an elevated white blood cell (WBC) count (WBC > 12,500); (e) evidence of obstructive jaundice (dilated common bile duct, bilirubin level > 3.0 mg/dl, or preoperative choledocholithiasis); (f) a history of biliary tract surgery, pancreatitis, hepatic disease, or prosthetic valves; and (g) patient determined to be at increased risk for infection secondary to his or her medical condition.

The criterion for inclusion in the protocol consisted of the absence of any of these conditions. Infectious complications were defined as pyrexia with a body temperature > 38°C twice a day (excluding the 1st postoperative day) and culture findings positive for pathogens from infectious sites such as wounds, the urinary or respiratory tract, and the abdominal cavity. If bacteria were found in the culture, a sensitivity to antimicrobial drugs was established. Antibiotics selected by the bacteriological test were administered to patients who fulfilled the criteria for sepsis. Antibiotic therapy was given until there was no evidence of intraabdominal or wound infection or persistent signs of sepsis. Suture abscesses were excluded if inflammation or discharge was minimal or confined to points of penetration and the incision healed without drainage or antibiotics.

Data were analyzed using the SPSS 10.0 statistical package for Microsoft Windows 98 (SPSS, Chicago, IL, USA). All frequency data were compared using the chi-square test with Yates' correction. Continuous variables were composed using a two-tailed unpaired *t*-test. Nominal variables were compared using Fisher's exact test. Significance was accepted at *p* < 0.05.

Table 2. Number (%) of organisms isolated

Name of organism isolated	Frequency
<i>Klebsiella oxytoca</i>	3 (25%)
<i>Pseudomonas aeruginosa</i>	2 (16.6%)
<i>Pseudomonas</i> spp.	2 (16.6%)
<i>Citrobacter freundii</i>	1 (8.3%)
<i>Escherichia coli</i>	2 (16.6%)
<i>Streptococcus viridans</i>	1 (8.3%)
<i>Staphylococcus aureus</i>	1 (8.3%)
Monobacterial	8
Mixed flora	2

Results

A total of 112 consecutive patients (42 male, 70 female) underwent elective LC over a 14-month period. Twenty patients were excluded from the statistical analysis for protocol violations. Group A included 49 patients; group B had 43. The overall preoperative status and demographics were similar for the two groups (Table 1).

The overall rate of postoperative infective complications was two of 92 (2.1%); both complications were wound infections. One infection occurred in the antibiotic prophylaxis group, for an infection rate of one of 49 (2.04%). In the group not receiving antibiotics, there was one infection, for an infection rate of one of 43 (2.32%). There was no statistical difference between the two groups in terms of infective complications.

Results from the culture of bile samples, which was performed in all patients, were positive in five patients (10.2%) in group A and five patients (11.6%) in group B. The results of eight of the positive cultures were monobacterial, and two organisms grew in two cultures. The type and incidence of bacteria cultured are shown in Table 2.

The most frequently isolated microorganism was *Pseudomonas* (33.3%), followed by *Klebsiella* (25%). In the patients who developed a septic complication, the bile cultures were negative. There was no correlation between bile microbiology and the postoperative infective complications. The two patients with infective complications of same magnitude were considered together and compared with the 90 patients who had no infective problems (Table 3). The multivariate analysis identified age (*p* < 0.001), presence of diabetes mellitus (*p* < 0.001), and an episode of colic within 30 days prior to surgery (*p* < 0.001) as independent factors significantly associated with the onset of infective complications. Neither antibiotic prophylaxis nor intraoperative perforation of the gallbladder leading to the spillage of bile and stones was significant.

Discussion

A recent meta-analysis determined that the mortality and complication rates are quite low for LC [7]. Nevertheless, the recent increase in the volume of LC raises important questions concerning the rate of infection and the use of preoperative antibiotic prophylaxis for this minimally invasive procedure.

Table 3. Risk factors for infective complications

	Infective complication (n = 2)	No complication (n = 90)	p value
Age, yr	63.5 ± 2.5	48.9 ± 8.1	< % _∞ 0.001
Weight, kg	70.5 ± 2.5	72.7 ± 6.2	NS
DOS, min	70.6 ± 9.8	71.8 ± 20.2	NS
Antibiotic intake	1/2	48/90	NS
Colic ^a	2/2	2/90	< % _∞ 0.001
Gallbladder rupture	0/2	14/90	NS
Bile spillage	0/2	18/90	NS
Stone spillage	0/2	6/90	NS
Diabetes mellitus	2/2	9/90	< % _∞ 0.001
Infected bile	0/2	10/90	NS

NS, not significant; DOS, duration of surgery

Results compared using *t*-tests for continuous variables and Fisher's exact test (because of small cell sizes)

^a Episode of colic within 30 days before surgery

Several studies have concluded that in open cholecystectomy the use of prophylactic antibiotics leads to a significant decrease in infective complications [6]. However, these data cannot be extrapolated to elective LC, and a review of the literature yielded little information on this subject.

Higgins et al. [2] found no reduction in infection rates when a single dose of prophylactic antibiotics was administered to patients undergoing elective LC. In a study that compared the use of three preoperative doses of cefazolin with no use of antibiotics patients undergoing elective LC, Illig et al. [4] reported similar results.

Tocchi et al. [10] followed up 84 patients undergoing elective LC for 2 years and found that in patients undergoing elective LC, antibiotic prophylaxis can be justified only in patients who have had episodes of colic within 30 days of surgery and patients with diabetes. In all other cases, antibiotic prophylaxis does not seem to affect the incidence of postoperative infections. In addition, McGuckin et al. [5] have recommended that antimicrobial prophylaxis only be used in high-risk patients.

Our data indicate that there are several risk factors that are significantly associated with an increased incidence of infective complications in patients who undergo elective LC. These risk factors include age > 60 years, the presence of diabetes mellitus, and episodes of colic within 30 days of surgery. Old age is also sometimes considered to be a risk factor for the development of infective complications after laparotomy, which may explain why during laparoscopic operations, stress hormones increase as immunosuppression decreases [1].

Tierney et al. [9] have suggested that the spasm phenomena that occur in the course of biliary colic, causing an increase in intraluminal pressure and biliary stasis, are serious risk factors for the onset of infectious processes. Furthermore, in diabetic patients with autonomic neuropathy, the motility of common bile duct muscles is altered; according to Ikard, that is likely to be why the risk of biliary sepsis is increased in these patients [3].

The results of the present study also illustrate the following important points: (a) There is no correlation between bile microbiology and postoperative infective

complications; (b) although spillage occurred in 19.5% of our patients, there was no correlation between the spillage and septic complications; (c) eliminating prophylactic antibiotics in low-risk patients undergoing elective LC would provide a direct cost savings, the disadvantages of antibiotic use—such as side effects including hypersensitivity and superinfection with *Clostridium difficile*—would be reduced, and there would be no induction of bacterial resistance.

Thus, patients undergoing elective LC, antibiotic prophylaxis seems justified only in high-risk patients. In all other patients, antibiotic prophylaxis does not seem to affect the incidence of postoperative infective complications. In low-risk patients, eliminating the unnecessary use of prophylactic antibiotics would result in a cost reduction, a lower risk of adverse reaction, and the reduction of microbial resistance.

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