The Need for Antibiotic Prophylaxis in Elective Laparoscopic Cholecystectomy

A Prospective Randomized Study

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**Hypothesis:** The need for antibiotic treatment when performing elective laparoscopic cholecystectomy may not be as important as it is thought. This study assesses the real efficacy of antibiotic prophylaxis in elective laparoscopic cholecystectomy with respect to the postoperative infection rate.

**Design:** A prospective randomized study on the routine use of antibiotic prophylaxis in laparoscopic cholecystectomy.

**Setting:** University teaching hospital, La Sapienza, Italy.

**Patients:** Eighty-four patients randomly placed into 2 groups (A [n = 44] and B [n = 40]) immediately before undergoing laparoscopic cholecystectomy.

**Methods:** Before anesthesia was administered, group A received intravenously 2 g of cefotaxime sodium diluted in 100 mL of isotonic sodium chloride solution; group B, 10 mL of isotonic sodium chloride solution in 100 mL of saline. A gallbladder bile sample for culture was withdrawn intraoperatively from all patients. In both groups, age, sex, weight, duration of surgery, presence of diabetes, American Society of Anesthesiologists patient classification score, preoperative autologous blood donation, antibiotic administration, intraoperative gallbladder rupture, findings from bile culture positive for bacteria, episodes of colic within 30 days before surgery, length of postoperative hospital stay, and number of septic complications were recorded. All data were correlated by univariate and multivariate analyses with the onset of septic phenomena.

**Results:** In group A, 3 cases of wound infection, 1 case of subhepatic abscess from bile leakage, and 1 case of urinary tract infection were observed; group B, 4 cases of wound infection, 1 case of bronchopneumonia, and 2 cases of urinary tract infection. Comparison of data showed no statistically significant difference between the groups. Findings from bile examination in patients with sepsis complications were positive in 5 patients in group A and in 6 in group B ($P = .91$). Multivariate analysis showed diabetes mellitus and colic episodes within 30 days before surgery as independent factors significantly associated to the onset of infectious complications.

**Conclusions:** In elective laparoscopic cholecystectomy, antibiotic treatment did not seem to affect the incidence and severity of infections or the degree of bile contamination.

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**ANTIBIOTIC prophylaxis,** which was introduced in the early 1960s, has been shown to markedly decrease the incidence of septic complications in biliary surgery, with the published rate ranging from 0% to 4%.1,2 Similarly satisfactory results have been achieved more recently with the intravenous bolus injection of antibiotics after the administration of anesthesia.3,4 Even if laparoscopic surgery, among other advantageous techniques, resulted in a marked decrease in the incidence of perioperative septic complications,5,6 antibiotic prophylaxis is routinely performed, though there are questions as to whether it is required or useful.7,8 The aim of this study was to test the efficacy of antibiotic prophylaxis in elective laparoscopic cholecystectomy.

**RESULTS**

Six patients were excluded from the original group. Group A included 44 patients; group B, 40. Data from the 2 groups were shown to be homogeneous for sex, age, weight, clinical condition (American Society of Anesthesiologists patient classification score), diabetes status, duration of surgery, number of intraoperative gall-

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PATIENTS, MATERIALS, AND METHODS

This prospective, computed-matrix, randomized study included 90 patients who underwent laparoscopic cholecystectomy from 1995 through 1997. Exclusion criteria were antibiotic intake in the 7 days before surgery; active, acute cholecystitis in the 6 months prior to admission; regular corticosteroid therapy; serum γ-glutamyltransferase, alkaline phosphatase, or direct bilirubin levels twice the reference levels of test kits (Ortho-Clinical Diagnostic; J & J Italy, Milan) used by the laboratory; endoscopic retrograde cholangiopancreatography–treated choledocholithiasis; and cardiac prostheses. Also, patients in whom laparoscopy was replaced by laparotomy were excluded. All enrolled patients gave their informed consent and were evaluated based on the American Society of Anesthesiologists patient classification score. Patients were then randomized into 2 groups (A and B). Thirty minutes before anesthesia was administered and again 24 hours after surgery, group A received 2 g of cefotaxime sodium diluted in 100 mL of isotonic sodium chloride solution. Group B received 10 mL of isotonic sodium chloride solution in 100 mL of saline. The surgical team was blinded to patients’ groups.

On the day of surgery, all patients underwent body cleansing with povidone-iodine soap and depilation with depilatory cream. At surgery, the skin was cleansed with 10% povidone-iodine solution. Cholecystectomy was performed according to the procedure previously reported.9 Gallbladder extraction from the peritoneal cavity was performed through the opening of the trocar positioned in the umbilical region, always without the use of an endoscope. The umbilical cut was sutured with a 2-0 nonabsorbable monofilament suture, whereas a 3-0 monofilament suture was used for the other incisions. The subhepatic region was drained through the opening of the trocar with a 5-mm silicone tube positioned in the right iliac fossa and removed on the first postoperative day. Although bile effusion and/or stones in the peritoneal cavity during surgery did not represent a reason for exclusion, their presence was always recorded. In these cases, the stones were removed, and peritoneal lavage was performed with 2000 mL of isotonic sodium chloride solution mixed with 1000 IU of heparin.

Antithrombotic prophylaxis was not performed, and a vesical catheter was never applied. The nasogastric tube was positioned at the start of surgery and removed at its conclusion. In all cases, at the start of surgery, a sample of bile was withdrawn by direct gallbladder puncture for culturing anaerobes and aerobes. As in previous reports, infectious complications were defined as pyrexia with a body temperature higher than 38°C twice a day (excluding the first postoperative day) and culture findings positive for pathogens from infectious sites such as wounds, the urinary or respiratory tract, and the abdominal cavity.10 If bacteria were found in the culture, the sensitivity to antimicrobial drugs was determined. Intra-abdominal collections were drained by ultrasonography-guided percutaneous drainage. Cefotaxime or antibiotics selected on the bacteriological test were administered to patients fulfilling criteria for sepsis. Antibiotic therapy was given until there was no evidence of intra-abdominal or wound infection or persistent signs of sepsis. Patients were followed up 1, 2, 3, and 4 weeks postoperatively. Further follow-up was made by telephone interview 6 weeks after surgery.

The statistical analysis of data performed by computer program (5.1G, Statistics/W; Statsoft Italia, Padova, Italy) was based on the χ2 test with Yates correction or t test, when applicable. Multivariate analysis was carried out with the stepwise logistic regression test using the onset of infectious complications as the dependent variable.

bladder ruptures, mean postoperative hospital stay, number of patients with episodes of colic within 30 days before admission, preoperative autologous blood donation, and percentage of infected bile (Table 1). In group A, 5 patients (11.3%) with infectious complications (3 with wound infections in the umbilical port, 1 with urinary tract infection, and 1 with subhepatic abscess secondary to bile leakage owing to loss of the clips positioned on the cystic duct) were observed. Diagnosis was established on the second postoperative day with findings from dimethyl iminodiacetic acid examination showing bile effusion through the stump of the cystic duct. Findings from subsequent abdominal ultrasonography confirmed the presence of a subhepatic collection treated with ultrasonography-guided percutaneous drainage. Culture findings of subhepatic fluid were positive for candidiasis. In group B, 7 patients (17.5%) showed infectious complications (4 with wound infections in the umbilical port, 1 with bronchopneumonia treated with specific antibiotic therapy, and 2 with urinary tract infections). The difference in the number of infections observed in the 2 groups was not statistically significant. Findings from cultures of bile samples, which were performed in all patients, were positive in 18 patients (40.9%) in group A and in 17 (42.5%) in group B. In 24 cases, a single microorganism was isolated, whereas in 11 cases, several microorganisms were present concomitantly. The most frequently isolated microorganism was *Escherichia coli* (37%) followed by *Klebsiella* (25.7%) (Table 2).

Of patients in whom a septic complication occurred, bile cultures were positive for organisms in 5 patients from group A and in 6 from group B (P = .91). The microorganisms present in the bile were different from those identified in the pus, except in 1 patient in group B (P = .99). The multivariate analysis identified diabetes mellitus and an episode of colic within 30 days before surgery as independent factors significantly associated with the onset of infectious complications (P < .001); age (P = .07) and antibiotic intake (P = .27) were not significant.

Antibiotic therapy has played a major role in the treatment of general and biliary septic complications in biliary surgery.11 The administration modalities of these drugs have progressively been changed, with preoperative prophylaxis preferred to postoperative treatment based on a number of studies that documented the efficacy of the former in controlling septic complications.
At present, laparoscopy is almost always used in elective cholecystectomy.\textsuperscript{11,13} The main advantages of this procedure include less postoperative pain, shorter hospital stays, a more rapid resumption of food intake and work, and a considerable decrease in perioperative sepsis complications.\textsuperscript{15,16} Despite the last observation, the same criteria of antibiotic prophylaxis previously applied to conventional surgery are routinely used for laparoscopic surgery, even though its actual need has not been ascertained.\textsuperscript{17-19}

Comparison of the 2 groups showed a higher number of complications in group B than in group A; however, this difference was not statistically significant. The nature and severity of complications in the 2 groups can be considered similar, except for a patient with diabetes in group A who suffered a subhepatic abscess caused by technical problems. Therefore, based on this study, antibiotic treatment does not seem to affect the incidence and severity of infections or the degree of bile contamination.

For a long time, geriatric age was considered a risk factor for the appearance of septic complications in the postoperative course of laparotomy.\textsuperscript{20} The multivariate analysis did not confirm this correlation as statistically significant, even though the incidence of infections in patients older than 65 years was higher compared with that of the remaining population. The relatively minor surgical trauma, earlier patient mobilization, and prompt resumption of nutrition allowed by laparoscopy are responsible for the decreased incidence of complications of sepsis in these patients. Furthermore, recent experimental studies have documented that during videolaparoscopy operations, stress hormones increase while immunosuppression decreases.\textsuperscript{21,22}

The ascertained presence of pathogens in the bile and the incidental rupture of the gallbladder during surgery were also independent of postoperative sepsis complications because these rare cases were sustained by microorganisms different from those present in the bile. The only variables significantly correlated with the onset of postoperative sepsis complications were a recent history of episodes of colic and concomitant diabetes. It is well known that in different pathological conditions affecting the biliary tract, an impeded bile flow facilitates the development of bacteriobilia and biliary sepsis.\textsuperscript{23-25} Spasm phenomena occurring in the course of biliary colic and causing an increase of intraluminal pressure and biliary stasis\textsuperscript{26,27} are real risk factors for the onset of infectious processes.\textsuperscript{28} The altered motility of common bile duct muscles, which is secondary to autonomic neuropathy observed in diabetic patients, as well as increased lipid concentration in the bile, are additional elements that can cause an increased susceptibility to biliary sepsis in patients with diabetes.\textsuperscript{29,30}

In patients undergoing elective laparoscopic cholecystectomy, antibiotic prophylaxis seems justified only in patients having episodes of colic within 30 days of surgery and in patients with diabetes. In all the other cases, antibiotic prophylaxis does not seem to affect the incidence of postoperative infections.

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REFERENCES

There are some interesting aspects we can comment on regarding the study by Tocchi et al. First, the authors present a very small group of patients with a problem that is frequently encountered all over the world. We should be reading about hundreds of patients receiving antibiotics and hundreds not receiving them instead of such small groups. Second, the infection rate seems exceedingly high in this selected group of patients (many exclusion criteria) who underwent elective, minimally invasive surgery. (Perhaps more so in the control group, but it is also high in the protected group.)

One wonders not necessarily about the usefulness of prophylactic antibiotics but about the surgical care protocols at the center where the study was performed. Perhaps there were several surgeons involved, maybe drains were being left, etc. Third, it is strange that in a selected population without acute cholecystitis the authors found bacterial contamination in more than 40% of bile samples. We do not know if the biliary tract was manipulated before surgery.

Many articles have proved that in elective biliary tract surgery, the use of prophylactic antibiotics produces a decline in the rate of postoperative infections. However, in this report, with a very select group of patients, minimally invasive intervention, and prophylactic protection, the postoperative infection rate is above what is expected. At our center we performed a prospective, comparative study1 administering 2 different groups of prophylactic antibiotics to patients with biliary tract problems (lithiasis) who underwent open and laparoscopic procedures; our protected group did not have any infection at all (the number of patients was similar to that of these authors).

We find it inappropriate and dangerous to conclude that the use of prophylactic antibiotics in those patients is not beneficial. Perhaps it would be better to try to find out what happened in such a select group of patients to develop such a high percentage rate of postoperative infections. Despite the results, we must acknowledge that the study by Tocchi et al is a well-designed, prospective, controlled, randomized trial; and we should be able to sustain this thought: because the infection rate is so low, we do not need prophylactic antibiotics. However, this is not the case with the present report.

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