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Microbiological assessment of bile during cholecystectomy: is all bile infected?

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Abstract

Aims. To determine the prevalence of bactibilia in patients undergoing cholecystectomy and to relate the presence or absence of organisms to the preoperative and postoperative course. *Patients and methods.* Patients undergoing cholecystectomy under the care of a single consultant surgeon during a continuous 5-year period were identified from a prospectively maintained departmental database. Symptoms, clinical signs, findings of investigations, details of treatment and postoperative care were noted. Risk factors for bactibilia (acute cholecystitis, common duct stones, emergency surgery, intraoperative findings and age >70 years) were documented. Patients were divided according to the presence (B+) or absence (B–) of bacteria on culture of their bile. *Results.* In all, 128/180 (70%) of cholecystectomies had full data available for analysis. Bacteria were identified in the bile of 20 (15.6%) patients (B+ group). The B+ group was significantly older at 63.78 ± 9.7 versus 61.62 ± 13.9 ($p < 0.05$) and contained significantly fewer females than the B– group ($p < 0.05$). All 20 patients (100%) in the B+ group had ≥ 1 risk factor, while these factors were present in only 29/108 (30.3%) of patients in the B– group ($p < 0.05$). The overall incidence of infective complications was 20% in the B+ group compared with 0.9% in the B– group ($p < 0.05$) and the bile-related infections were higher in the B+ group ($p < 0.05$). *Conclusions.* The study demonstrated that while patients with complicated gallstone disease frequently exhibit bactibilia, patients with uncomplicated cholelithiasis have aseptic bile. The findings would suggest that prophylactic antibiotics should be limited to patients with risk factors for bactibilia.

Key Words: *Cholelithiasis, bactibilia, cholecystectomy, antibiotic prophylaxis*

Introduction

Despite recommendation from the Scottish Intercollegiate Guidelines Network (SIGN) [1] that they should not be prescribed, most patients undergoing laparoscopic cholecystectomy will receive a single dose of prophylactic antibiotics on induction of anaesthesia. The SIGN guidelines identified only four papers that had set out to assess the role of antibiotic prophylaxis in laparoscopic cholecystectomy [2–5]. Although none of the studies identified was actually a randomized trial of antibiotics versus no antibiotics, the indirect evidence suggested that no antibiotics were required for a laparoscopic cholecystectomy. Since the SIGN review, six randomized controlled trials have compared antibiotics with no antibiotics in elective laparoscopic cholecystectomy and all have concluded that antibiotics are not required [6–11].

This advice is contrary to that given by Meijer and colleagues [12] in a meta-analysis of trials of antibiotic prophylaxis in open biliary tract surgery published in 1990. From the results of 42 trials looking at the effects of antibiotic prophylaxis in the prevention of wound infection, they suggested that there was an overall 9% benefit in favour of antibiotic prophylaxis. When high-risk patients were analysed as a subgroup, the benefit of prophylaxis was greater. The paper concluded that antibiotic prophylaxis should be administered.

There are several reasons for these differing conclusions. Firstly, since most post-cholecystectomy infections are wound infections, it is logical that the risk of infection in the smaller laparoscopic wounds would be less than in a traditional Kocher incision. A study of 341 consecutive cases noted a significantly higher infection rate for open compared with laparoscopic cholecystectomy (12.9% versus 1.8%; $p < 0.001$) [5].

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Another important point worthy of consideration is the biliary case mix. It is well known that bactibilia is a common finding in high-risk individuals with complicated gallstone disease, including those with biliary obstruction, age >70 years, acute cholecystitis, common bile duct stones, cholangitis and non-functioning gallbladders [13–16]. These factors, together with the use of biliary stents [17,18], are the major risk factors for postoperative wound infection following biliary surgery. However, there are relatively few data on the prevalence of bactibilia in patients undergoing cholecystectomy for simple cholelithiasis.

Even if there is evidence of bactibilia – is it the cause of postoperative infections? In infected bile, the typical pathogens are the Gram-negative enteric aerobes such as *Escherichia coli*, *Klebsiella* spp. and *Proteus* spp., while *Pseudomonas aeruginosa*, *Bacteroides fragilis* and *Enterococcus faecalis* are less commonly cultured [18]. To justify antibiotic prophylaxis against biliary organisms, it requires to be shown that the bile is colonized with bacteria and that the same bacteria are the causative organisms of postoperative infections.

The aim of this study therefore was to determine the prevalence of bactibilia in patients undergoing cholecystectomy, for both simple and complicated gallstone disease, so as to document the type of organisms present and to relate these findings to the nature of, and organisms cultured in postoperative infections.

Patients and methods

All patients undergoing cholecystectomy under the care of a single consultant general surgeon during a continuous 5-year period were identified from a prospectively maintained departmental database.

Patient notes were reviewed to determine demographic data together with symptoms and clinical findings at the time of referral by the general practitioner and at all subsequent elective and emergency hospital admissions up until the time of definitive treatment by means of cholecystectomy. Patients were classified as simple gallstone disease (biliary colic) or complicated gallstone disease (acute cholecystitis, obstructive jaundice due to common duct stones, pancreatitis). Patients' full blood counts and liver function tests were documented, as were results of radiological investigations including ultrasound scans and, when performed, the indication and findings of endoscopic retrograde cholangiopancreatography (ERCP) were noted.

Data on the indication for, urgency and type of cholecystectomy performed (laparoscopic/open/conversion) were collected, as were intraoperative findings such as significant adhesions and the presence of pus within the gallbladder or adjacent tissues.

All patients received a single dose of cefuroxime 750 mg and metronidazole 500 mg intravenously following induction of anaesthesia.

The results of bile cultures performed at the time of cholecystectomy were collated and all microbiologically confirmed postoperative infections were identified from the microbiology department computerized database.

Patients were grouped according to the presence (B+) or absence (B–) of bacteria cultured from the bile. Both groups were then analysed according to the presence or absence of known risk factors for bactibilia including: age >70 years, diagnosis of acute cholecystitis, presence of common duct stones, the need for emergency surgery and the presence of adverse intraoperative findings.

Details of infections treated by general practitioners were noted at the time of postoperative review in the outpatient department. Wound scars were also examined for the presence of infection at this time.

Data were compared using the χ^2 test and statistical significance was taken at the 5% level.

Results

During the period of the study 180 cholecystectomies were performed, of which 128 (70%) had full data available for analysis. Following laboratory culture, bacteria were identified in the bile of 20 (15.6%) patients. Patients with bacteria present (B+) were compared with the group with no bacteria (B–) present on bile culture. The demographic data for the two groups are shown in Table I. The B+ group

Table I. Demographic features, preoperative diagnoses and management according to the presence or absence of bacteria on bile culture.

Parameter	Bacteria present 20 (15.6%)	Bacteria absent 108 (84.4%)
Demographics		
Age ± SD	63.78 ± 9.7*	51.62 ± 13.88
Gender ratio (F:M)	1.85*	3.7
Diagnosis		
Biliary colic/chronic cholecystitis	9 (45%)	93 (86%)
Acute cholecystitis	4* (20%)	4 (3.7%)
Gallstone pancreatitis	2* (10%)	6 (5.5%)
Obstructive jaundice	5* (25%)	5 (4.6%)
Biliary intervention		
ERCP	6 (30%)	9 (83%)
Urgency		
Routine	15 (75%)	106 (98.1%)
Emergency	5* (25%)	2 (1.9%)
Type of procedure		
Laparoscopic	7 (35%)	86 (79.6%)
Conversion	3* (15%)	7 (6.5%)
Open	10* (50%)	15 (13.9%)

*$p < 0.05$ for bacteria present versus organisms absent (χ^2 test).

was found to be significantly older at 63.78 ± 9.7 versus 61.62 ± 13.9 ($p < 0.05$). There were also significantly fewer females in the B+ group, with a female to male ratio of 1.85 versus 3.7 for the B– group ($p < 0.05$).

Patients in the B+ group had a greater proportion of acute presentations (acute cholecystitis, gallstone pancreatitis and obstructive jaundice) than the B– group ($p < 0.05$). The majority of patients in each group who could have benefited from ERCP received this intervention. A higher proportion of patients in the B+ group required urgent intervention and this group also underwent a greater proportion of open procedures and conversions from laparoscopic to open cholecystectomy ($p < 0.05$).

The prevalence of risks factors for bactibilia for the two groups is summarized in Table II. All 20 patients (100%) in the B+ group had at least one risk factor for bactibilia, while these factors were present in only 29/108 (30.3%) of patients without bacteria in their bile ($p < 0.05$).

The prevalence of infective complications for the two groups is summarized in Table III. The overall incidence of infective complications was 20% in the B+ group compared with 0.9% in the B– group ($p < 0.05$). The infections in the B+ group consisted of three wound infections, one infection from drain fluid and one from bile draining from a T-tube, while in the B– group there was a single urinary tract infection. In the B+ group, the two wound infections were related to *Staphylococcus aureus*, while the bile and drain fluid grew *Escherichia coli* and *Klebsiella* spp., respectively. In the B– group, the single urinary tract infection was due to *Proteus* spp.

Table II. Risk factors for bactibilia in patients with and without bacteria present in their bile.

Parameter	Bacteria present 20 (15.6%)	Bacteria absent 108 (84.4%)
Risk factors for bactibilia		
Acute cholecystitis	4 (20%)*	4 (4.3%)
Common duct stones	5 (25%)*	11 (10.8%)
Emergency surgery	5 (25%)*	2 (2.2%)
Intraoperative findings	5 (20%)*	7 (7.6%)
Age >70 years	1 (5%)	5 (5.4%)
Overall proportion with risk factors for bactibilia	20 (100%)*	29 (30.3%)

*$p < 0.05$ for bacteria present versus organisms absent (χ^2 test).

Table III. Postoperative infections in patients with and without bacteria present in their bile.

Infective complications	Bacteria present 20 (15.6%)	Bacteria absent 108 (84.4%)
Overall	4 (20%)*	1 (0.9%)
Bile-related	2 (10%)*	0 (0%)

*$p < 0.05$ for bacteria present versus organisms absent (χ^2 test).

Discussion

The primary finding of the study was that the overall prevalence of viable bacteria within bile sampled at cholecystectomy was 15.6%. All patients with bactibilia had a risk factor for biliary colonization and in 19 of 20 cases this included the presence of complex gallstone disease, the remaining case being on grounds of age alone. By comparison of 108 patients in the group without colonization, the vast majority (84/108) of patients had simple gallstone disease with no evidence of history of acute cholecystitis or common duct stones and no requirement for emergency surgery. Thus in the absence of a risk factor, bacteria are unlikely to be found colonizing the bile.

A further interesting but unexplained finding is the reduction in the female predominance in those with bactibilia. Cholelithiasis is characteristically a disease of middle-aged women and the gender ratio in the B– group is typical of the ratio identified in the published literature [19]. However, in the B+ group the ratio was halved from 3.7:1 to 1.85:1.

Several studies have documented the nature of biliary organisms and defined infection rates in patients with complex gallstone disease [13–18]. In contrast, relatively few studies have looked at bile from patients who do not have evidence of gallstones. A study by Csendes et al. [20] compared the prevalence of bactibilia in normal controls (gastric ulcer surgery) to patients undergoing cholecystectomy for acute and chronic cholecystitis. They found that all controls had sterile bile while those with acute and chronic cholecystitis had positive cultures in 47% and 30% of cases, respectively.

The identification of viable bacteria in bile of patients with chronic cholecystitis is in keeping with studies performed by Pitt and colleagues, who showed that treatment with antibiotics does not render infected bile sterile [21]. This may explain why patients with acute cholecystitis often re-present with identical signs and symptoms if a cholecystectomy is not performed at the index admission despite administration of antibiotics.

It may be argued that our administration of antibiotics may have adversely biased the positive culture rates of the bile. Antibiotics were administered following induction of anaesthesia in all cases, in accordance with published recommendations [22]. However, as the average cholecystectomy lasted little over 30 min, then it is unlikely that a single prophylactic dose of antibiotics would be efficacious against all bacteria present within the bile during this time frame.

Another consideration is that the antibiotics may have influenced the incidence of postoperative infections. Had this been the case, then it would be likely that the effect would have been comparable for the two groups. Furthermore, for the organism-negative

group, any infection must develop from a source other than bile. In such cases it may be argued that if prophylactic antibiotics are to be prescribed then they should be directed towards skin flora such as *S. aureus* and not biliary organisms. Hambraeus et al. noted a significant difference in wound infection rates in patients with and without bactibilia at 12.8% versus 3.2%, respectively. Furthermore, infections with *S. aureus* were as common as *E. coli* and were the predominant bacteria in patients without evidence of bactibilia [23]. Harling et al. reported interesting results in a randomized trial of antibiotics versus bag extraction and no antibiotic prophylaxis in patients undergoing cholecystectomy [24]. They noted three infections in each group, all due to infections by skin commensals, and concluded that septic sequelae of uncomplicated laparoscopic cholecystectomy were uncommon but were not entirely prevented by antibiotic or mechanical prophylaxis.

Taken together, the evidence would suggest that routine antibiotic prophylaxis is not required for patients with cholelithiasis unless a risk factor for bactibilia is identified. For patients in whom a risk factor is noted preoperatively or in whom an intraoperative risk factor is identified then prophylaxis is recommended with broad-spectrum antibiotic cover to include both typical biliary flora and skin commensals.

Conclusions

The study has demonstrated that while patients with complicated gallstone disease frequently exhibit bactibilia, patients with uncomplicated cholelithiasis have aseptic bile. Therefore, there is a strong argument that unless a risk factor for bactibilia is identified then no 'prophylactic' antibiotic should be prescribed. This would reduce prescriptions by 60% and would have the combined effects of reducing cost, lessening the occurrence of adverse drug effects and reducing the development of antibiotic resistance. If a patient from this group develops a wound infection it should be cultured and treated with an anti-staphylococcal antibiotic in the first instance. On the other hand, patients with a risk factor for bactibilia should continue to receive prophylaxis prior to their operation.

References

[1] Scottish Intercollegiate Guidelines Network. Antibiotic prophylaxis in surgery. SIGN, July 2000.

[2] Frantzides CT, Sykes A. A reevaluation of antibiotic prophylaxis in laparoscopic cholecystectomy. J Laparoendosc Surg 1994;4:375–8.

[3] Watkin DSA, Wainwright AM, Thompson MH, Leaper DJ. Infection after laparoscopic cholecystectomy: are antibiotics really necessary? Eur J Surg 1995;161:509–11.

[4] den Hoed PT, Boelhouwer RU, Veeh HF, Hop WC, Bruining HA. Infections and bacteriological data after laparoscopic and open gallbladder surgery. J Hosp Infect 1998;39:27–37.

[5] Garcia N, Kapur S, McClane J, Davis JM. Surgical infections and prophylactic antibiotics: 341 consecutive cases of gallbladder surgery in the era of laparoscopic surgery. J Laparoendosc Adv Surg Tech A 1997;7:157–62.

[6] Illig KA, Schmidt E, Cavanaugh J, Krusch D, Sax HC. Are prophylactic antibiotic required for elective laparoscopic cholecystectomy? J Am Coll Surg 1997;184:353–6.

[7] Dobay KJ, Freier DT, Albear P. The absent role of prophylactic antibiotics in low-risk patients undergoing laparoscopic cholecystectomy. Am Surg 1999;65:226–8.

[8] Higgins A, London J, Charland S, Ratzer E, Clark J, Haun W. Prophylactic antibiotic required for elective laparoscopic cholecystectomy? Arch Surg 1999;134:611–3.

[9] Mahatharadol V. A reevaluation of antibiotic prophylaxis in laparoscopic cholecystectomy: a randomised controlled trial. J Med Assoc Thai 2001;84:105–8.

[10] Tocchi A, Lepre L, Costa G, Liotta G, Mazzoni G, Maggiolini F. The need for antibiotic prophylaxis in elective laparoscopic cholecystectomy: a prospective randomized study. Arch Surg 2000;135:67–70.

[11] Koc M, Zulfikaroglu B, Kece C, Ozalp N. A prospective randomized study of prophylactic antibiotics in elective laparoscopic cholecystectomy? Surg Endosc 2003;17:1716–8.

[12] Meijer WS, Schmitz PI, Jeekel J. Meta-analysis of randomized, controlled trials of antibiotic prophylaxis in biliary tract surgery. Br J Surg 1990;77:283–90.

[13] Reiss R, Eliashiv A, Deutsch AA. Septic complications of bile cultures in 800 consecutive cholecystectomies. World J Surg 1982;6:195–9.

[14] Wells GR, Taylor EW, Lindsay G, Morton L. Relationship between bile colonisation, high-risk factors and postoperative sepsis in patients undergoing biliary tract operations whilst receiving prophylactic antibiotic. Br J Surg 1989;76:374–7.

[15] Thompson JE, Benninon RS, Doty JE, Muller EIL, Pitt HA.. Predictive factors of bactibilia in acute cholecystitis. Arch Surg 1990;125:261–4.

[16] Landau O, Kott I, Deutsch AA, Stelman E, Reiss R. Multifactorial analysis of septic bile and septic complications in biliary surgery. World J Surg 1992;16:962–5.

[17] Sung JY, Leung JWC, Shaffer EA, Lam K, Olson ME, Costerton JW, et al. Ascending infection of the biliary tract after surgical sphincterotomy and biliary stenting. J Gastroenterol Hepatol 1992;7:240–5.

[18] Lee DWH, Chung SCS. Biliary infection. Baillieres Clin Gastroenterol 1997;11:707–24.

[19] Diehl AK. Epidemiology and natural history of gallstone disease. Gastroenterol Clin North Am 1991;20:1–19.

[20] Csendes A, Fernandez M, Uribe P. Bacteriology of the gallbladder bile in normal subjects. Am J Surg 1975;129: 629–31.

[21] Pitt HA, Postier RG, Cameron JL. Biliary bacteria: significance and alterations after antibiotic therapy. Arch Surg 1982; 117:445–9.

[22] Classen DC, Evans RS, Pestonik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. N Engl J Med 1992;326:281–6.

[23] Hambraeus A, Laurell G, Nybacka O, Whyte W. Biliary tract surgery: a bacteriologic and epidemiologic study. Acta Chir Scand 1990;156:155–62.

[24] Harling R, Moorjani N, Perry C, MacGowan AP, Thompson MH. A prospective, randomized trial of prophylactic antibiotics versus bag extraction in the prophylaxis of wound infection in laparoscopic cholecystectomy. Ann R Coll Surg Engl 2000;82:408–10.