A selective antibiotic prophylaxis policy for laparoscopic cholecystectomy is effective in minimising infective complications

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ABSTRACT

INTRODUCTION It has been demonstrated previously that the identification of bactibilia during cholecystectomy is associated with the presence of one or more risk factors: acute cholecystitis, common duct stones, emergency surgery, intraoperative findings and age >70 years. Current evidence-based guidance on antibiotic prophylaxis during laparoscopic cholecystectomy (LC) is based on elective procedures and does not take into account these factors. The aim of this study was to assess the effectiveness of a selective antibiotic prophylaxis policy limited to high risk patients undergoing LC with the development of port site infections as the primary endpoint.

METHODS One hundred consecutive patients undergoing LC under the care of a single consultant surgeon during a one-year period were studied prospectively. Data collected included patient demographics (age, sex) as well as details of the history of gallstone disease to determine those with complex disease and risk factors for bactibilia. A single dose of antibiotics (second generation cephalosporin and metronidazole) was administered on induction to patients with a risk factor present. Information relating to all radiologically or microbiologically confirmed infections was documented.

RESULTS Eighty-four of the patients were female and the mean age was 47.7 ± 16.0 years. Nineteen LCs were performed as emergencies and the remainder were elective procedures. A risk factor for bactibilia was present in 35 patients. A wound infection was identified in four cases, two of which were *Staphylococcus aureus* (one methicillin resistant), one was a coagulase negative *Staphylococcus* and one wound cultured a mixed anaerobic growth. Three of the infections occurred in patients receiving prophylaxis (2 staphylococcal and 1 anaerobic) at intervals of 7, 14 and 19 days respectively. One patient with a body mass index of 32kg/m^2 in the 'no prophylaxis' group developed a coagulase negative staphylococcal infection at 10 days. No intra or extra-abdominal infections were identified.

CONCLUSIONS This study has demonstrated that restricting antibiotic prophylaxis to high risk patients has no detrimental effects in terms of increasing the rate of infections in those with no risk factors. Furthermore, the act of not prescribing to low risk patients will limit costs and the risk of adverse events. It will also reduce the risk of resistance and clostridial infections in this cohort.

KEYWORDS

Antibiotics – Bactibilia – Laparoscopic cholecystectomy

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Patients undergoing a laparoscopic cholecystectomy (LC) frequently receive a single dose of prophylactic antibiotics on induction of anaesthesia despite recommendations from the Scottish Intercollegiate Guidelines Network (SIGN)¹ to the contrary. The SIGN recommendations were based on analysis of four studies assessing the role of antibiotics in elective surgery^{2–5} and even though none of these papers were randomised controlled trials (RCTs), the indirect evidence was in favour of not prescribing prophylactic antibiotics in LC.⁶ Six RCTs have been published since the publication of the SIGN recommendations, all dealing with elective LC and all concluding that no prophylactic antibiotics are required.^{7–12}

Choudhary *et al* came to the same conclusion in a meta-analysis of nine RCTs published in 2008.¹³ They assessed 1,337 low risk patients undergoing LC and found no statistically significant reduction in the prevalence of: overall infectious complications ($p=0.20$), superficial wound infections ($p=0.36$), major infections ($p=0.97$), distant infections ($p=0.28$) or prolongation of hospital stay ($p=0.77$). Choudhary *et al* concluded their meta-analysis stating that prophylactic antibiotics do not prevent infections in low risk patients undergoing LC.¹³

As most surgeons are now familiar with the technique of LC, more and more urgent/emergency procedures are

being performed in patients with acute biliary disease. The literature on antibiotic prophylaxis in such cases is sparse for LC. However, in the open cholecystectomy era, in a meta-analysis of 42 trials, Maijer *et al* reported a 9% benefit in favour of antibiotics and found that this was greatest in those with high risk factors for bactibilia.¹⁴

The risk factors for bactibilia are well defined and include acute cholecystitis, common duct stones, emergency surgery, intraoperative findings and age >70 years.^{15–18} It has been demonstrated that all patients found to have bactibilia at the time of cholecystectomy have at least one of these risk factors and that patients with uncomplicated gallstone disease do not show evidence of bactibilia.⁶

The main aim of this study was to assess the effectiveness of a selective antibiotic prophylaxis policy limited to high risk patients undergoing LC with the development of port site infections as the primary endpoint.

Methods

One hundred consecutive patients who underwent successful LC under the care of a single consultant during a one-year period were studied prospectively. This study was designed to validate a previous one on the prevalence of bactibilia in patients undergoing cholecystectomy⁶ and to determine prospectively and accurately the prevalence of wound infections. As such, a power calculation was not attempted.

Both elective and emergency cases were included in the study. A standard four-port technique was applied and all gallbladders were retrieved in a bag. Patients who had a planned LC that was converted to an open procedure were excluded from the study. For those patients with a risk factor for bactibilia as identified in a previous study⁶ (acute cholecystitis, common duct stones, emergency surgery, intraoperative findings and age >70 years), a single dose of preoperative antibiotics (second generation cephalosporin and metronidazole) were administered at induction.

Data including patient demographics (age, sex) and relevant past medical history (particularly that of biliary disease) were obtained from the patients. Information regarding the perioperative period was collated from the patient notes, and postoperative data including visits to accident and emergency departments or the general practitioner were also documented. Microbiological data were obtained from the computerised hospital database and used to confirm the presence or absence of infections following the performance of wound swabs.

Results

The mean age of the study population was 47.7 ±16.0 years (range: 18–85 years). Eighty-four per cent of the patients were female.

Eighty-one procedures were performed electively and nineteen procedures were performed as emergencies for acute biliary disease. In addition, a further 16 cases had one or more risk factors for bactibilia, and so 35 patients were considered high risk for bactibilia and prescribed prophylactic antibiotics (Table 1).

Table 1 Indications for antibiotic prophylaxis in laparoscopic cholecystectomy (n=35)

Indication	Number of patients
<i>Emergency procedure</i>	
Acute cholecystitis	18 (51.4%)
Empyema	1 (2.9%)
<i>Elective procedure</i>	
Recent acute cholecystitis	5 (14.3%)
Recent obstructive jaundice	6 (17.1%)
Recent acute pancreatitis	2 (5.7%)
Age >70 years	3 (8.6%)

An infective complication was identified in only four cases, all of which were superficial wound infections. Three of the cases occurred in patients receiving antibiotic prophylaxis. In this group, the organisms cultured included two cases of *Staphylococcus aureus* (one methicillin resistant) and one of mixed anaerobic growth. These infections were detected at intervals of 7, 14 and 19 days respectively. The patient with a mixed anaerobic growth was a 66-year-old woman with a body mass index (BMI) of 38kg/m².

The one patient in the 'no prophylaxis' group to develop a wound infection was obese with a BMI of 32kg/m² and cultured a coagulase negative *Staphylococcus* ten days post-operatively. None of the patients who developed a wound infection had experienced gallbladder perforation or intra-abdominal bile spillage perioperatively.

Discussion

The primary finding of the study was that a selective antibiotic prophylaxis policy limited to those with risk factors for bactibilia minimises the rates of infective complications following LC. Of the four superficial wound infections detected, three occurred in patients receiving antibiotics. Furthermore, three were due to staphylococcal infections and occurred at 7, 10 and 14 days postoperatively. The nature of the isolated organisms and the extended interval following surgery suggest that the infections are unlikely to have arisen as a result of infected bile, and are more likely to represent colonisation and subsequent infection of the healing tissue by skin flora. Further supportive evidence for this statement arises from the fact that none of the patients experienced a bile leak and all gallbladders were retrieved intact in a bag.

The typical pathogens associated with bactibilia are the Gram negative enteric aerobes such as *Escherichia coli*, *Klebsiella* spp and *Proteus* spp while *Enterococcus faecalis*, *Pseudomonas aeruginosa* and *Bacteroides fragilis* are less commonly cultured.¹⁹ In only 1 case in this series was a mixed anaerobic growth identified, and this patient was obese and the infection occurred at 19 days following her surgery.

Our decision to prescribe prophylaxis to patients with risk factors for bactibilia is based on the fact that sepsis of

biliary origin carries significant morbidity.^{20–22} The 2008 update of the SIGN recommendations for antibiotic prophylaxis stated that it is considered good practice to give prophylactic antibiotics to high risk patients undergoing LC.²³ However, this was based on the clinical experience of the guidelines development group rather than evidence from the literature. As the current study is not a randomised trial of prophylaxis in high risk patients, it may be that the use of antibiotics could be reduced further.

One further area where the role of antibiotics is debated relates to the perforated gallbladder or spilled bile. In our cohort, none of the patients who developed superficial wound infection had endured bile spillage or traumatic perforation of the gallbladder perioperatively although this did occur in several of the patients undergoing cholecystectomy for acute biliary disease when the gallbladder was oedematous and friable. A study from 2008 suggested that even in such cases, there was no evidence that routine administration of antibiotics reduced the risk of wound infection except in cases of diabetic or elderly patients, or those with ASA (American Society of Anesthesiologists) grade ≥ 3 .²⁴

There are additional benefits to a selective policy based on prescribing antibiotics only to those with risk factors for bactibilia. Avoidance of antibiotics abolishes the risk of an allergic reaction and helps to lessen the risk of development of resistance. A further problem of escalating importance is that of *Clostridium difficile* infection and the development of pseudomembranous colitis with its consequential morbidity/mortality and prolonged hospital stay.²⁵ *C. difficile* infections usually arise following prolonged antibiotic therapy but are now linked increasingly to administration of 'prophylactic antibiotics' and of particular relevance to cholecystectomy is that of cephalosporins.^{26,27}

Moreover, in an era of ever increasing financial accountability, despite the cost of a standard prophylactic dose of antibiotics being in the order of £1, the fact that approximately 50,000 LCs are performed annually in the National Health Service every year²⁸ means that substantial savings are possible. In our experience, limiting the prophylaxis to high risk patients would reduce this expenditure by almost two-thirds. It is therefore in the clinicians', patients' and hospital managers' best interests not to prescribe prophylactic antibiotics unless deemed necessary on the basis of high risk criteria for bactibilia.

We now have prospective data on infection rates in a population with risk factors for bactibilia and, more importantly, data to suggest infections are very infrequent in patients with no risk factors. Indeed, the infection that did occur is unlikely to have been linked to the operation itself. We propose using this preliminary data to design and power a national multicentre RCT of the use of antibiotics in patients at risk of bactibilia.

Conclusions

Patients with risk factors for bactibilia including a current or recent history of acute cholecystitis, obstructive jaundice or acute biliary pancreatitis appear to benefit from prophylaxis, with a low rate of infective complications (most if not

all of which were unrelated to biliary organisms) suggesting that antibiotic prophylaxis in this group was effective. Furthermore, the identification of a wound infection in only 1 of 65 patients not receiving prophylaxis indicates, as recommended by the published guidelines, that antibiotics and their associated complications may be avoided without any detrimental effect in terms of infective complications following LC.

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Publication malpractice: salami publication

The editors have recently identified and halted publication of a paper that stepped over the limit of acceptable practice in reporting clinical results. Thanks to an alert reviewer (to whom we are grateful), it became clear that a clinical report included several patients who had also been reported by the authors in previous papers. Although some of these papers were cited in the submission to the *Annals*, the authors did not make clear in the paper the extent of overlap with their previous work. The patients had varying degrees of elbow stiffness or fixity after trauma and the papers described various subgroups, all treated with a hinged external fixator.

Following the review of this paper, which alerted us to possible ‘salami publication’ of the authors’ clinical material, we had a detailed correspondence with them. The authors were unable to satisfy us that their actions were justified by clinical differences. Crucially, they did not describe the extent of overlap with previous papers in the present submission. All intending authors should be aware that absolute transparency is required when publishing repeated observations on the same patients or when there is overlap in patient groups published separately. The reader should be able to understand how many patients were treated and when.

The editors have previously made clear our determination to maintain the highest possible standards of publication ethics. In the past, we have been made aware of duplicate publications, which is a clear breach of expected standards and which we have brought to the attention of the relevant authority. Authors are advised to review the guidelines published by the Committee on Publication Ethics, and, in case of any doubt, to discuss their proposed submission with the Editor at an early stage.

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