Postcholecystectomy Wound Infection

The Impact of Prophylactic Antibiotics on the Epidemiology of Infections

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The clinical courses of 347 patients undergoing gallbladder surgeries were monitored to study the epidemiology of postcholecystectomy wound infection in a hospital in which high-risk patients received prophylactic antibiotics. Overall, 3.8% of patients had wound infections. Patients who had positive bile cultures taken during surgery or positive intraoperative wound cultures had higher rates of infection than patients with negative cultures. However, there was a poor correlation among the bacterial isolates that were recovered from the bile or the wound surface during surgery and from postoperative infections. Antibiotic-sensitive enteric bacteria were recovered from bile samples at surgery, gram-positive organisms and enteric gram-negative bacteria were isolated from intraoperative cultures of the wound surface, and antibiotic-resistant gram-negative bacteria or enterococci were recovered from wounds that developed postoperative infections. There was a strong association between the prior receipt of prophylactic antibiotics and infections with antibiotic-resistant bacteria. Data suggest that bactibilia is still an important epidemiologic marker that identifies patients at high risk for subsequent wound infection. However, in patients who have received prophylactic antibiotics, intraoperative cultures cannot be relied on to guide the choice of empiric therapeutic antibiotics for postoperative infections. Bacteria responsible for these infections are not identified by cultures taken at the time of surgery and are often resistant to the class of antibiotics used for prophylaxis.

EXTENSIVE LITERATURE characterizes the epidemiology and risk factors for postoperative wound infections after gallbladder surgery.1-13 These studies document a strong association between the presence of bacteria in bile cultures taken at surgery and the occurrence of subsequent infection. Patients with bactibilia have a rate of wound infections that is 3–5 times greater than that of patients with negative intraoperative bile cultures. In several studies, there has been a strong correlation between the species of bacteria cultured during operation from bile and after operation from the infected wound.1-3,8,9,14-17 Some clinicians use the results of bile cultures taken during surgery to guide their choice of empiric therapeutic antibiotics for subsequent wound infections. However, most of the studies that had demonstrated an association between bactibilia and infection involved patients who had not received prophylactic antibiotics. Today, prophylactic antibiotics are prescribed for virtually all patients who are at risk for bactibilia or infection.

We hypothesized that the widespread use of prophylactic antibiotics might alter the association between bactibilia and infection in patients undergoing cholecystectomies. In the current study, we reevaluated the epidemiology of postcholecystectomy wound infections in a hospital where high-risk patients routinely receive prophylaxis. We found that intraoperative bile or wound cultures cannot be used to predict the etiologic agent responsible for postoperative infections or guide the choice of therapeutic antibiotics.

Methods

Between January 1982 and August 1984, we prospectively studied 347 patients undergoing gallbladder surgery at a 700-bed, university-affiliated hospital. Eligible patients were identified on the day of surgery from the operating room schedule. Patients scheduled for cholecystectomies, with or without intraoperative cholangiograms, were se-
lected for study. Patients who underwent surgery in which the gastrointestinal tract was entered were excluded from the final study population. On the day of surgery, a study nurse in the operating room collected epidemiologic information that defined risk factors for infection and made observations regarding the surgical procedure. This information included the patient's age, sex, history of prior biliary tract disease, clinical prognosis, and an assessment of the patient's preoperative physical status. The medical record was reviewed to identify patients with fever, elevated white blood cell count (WBC), or emergency admission to the hospital in the 3 days before surgery. The study nurse also noted perioperative and intraoperative risk factors such as the use of prophylactic antibiotics, surgical wound class, use of drains, length of surgery, and histopathologic features of the resected gallbladder.

During surgery, the study nurse collected semiquantitative cultures of the wound surface at the time of closure. A 5.0-μ Millipore filter (Millipore Corporation, Bedford, MA) was held in contact with the subcutaneous tissues for 5 seconds and then immediately cultured on trypticase soy agar with 5% sheep blood. Intraoperative cultures of bile were obtained at the discretion of the primary surgeon. These specimens were collected by the surgeon or by an operating room nurse after removal of the gallbladder. Bile cultures were collected on swabs and cultured aerobically by standard microbiologic techniques.

All patients were monitored after operation for the development of wound infections. The wound was considered to be infected if pus or purulent exudate was present. A study nurse visited each patient three times weekly for the duration of hospitalization to check the wound and monitor the occurrence of infections, initiation of therapeutic antibiotics, development of fever, duration of postoperative stay, or death. In addition, follow-up forms were sent to the attending surgeons to identify wound infections that occurred after hospital discharge. Statistical significance of differences between proportions was determined with chi-square statistics and Fisher's exact test.

Results

The Study Population

The study population comprised 347 patients. Their ages ranged from 15–87 years, with a mean of 52 years; 18% were older than 70 years. Seventy per cent of the patients were female. Most patients were relatively healthy; only 3% had fatal underlying diseases. The majority were in American Society of Anesthesiology (ASA) physical status groups 2 or 3. Ten per cent of the population had diabetes mellitus, but less than half of these were receiving insulin. Five per cent of patients had jaundice at the time of surgery and 2% had undergone prior biliary surgeries.

Clinical signs or symptoms suggestive of acute cholecystitis were present in 27% of patients; 10% had been admitted through the emergency room in the 3 days before surgery, 15% had preoperative WBC in excess of 10,000/mm³, and 5% had temperatures greater than 100.4 F within 24 hours of surgery. Acute cholecystitis was diagnosed histologically in 11% of specimens that were removed at surgery.

Preoperative antibiotics were administered to 64% of patients on the basis of risk factors or acute symptoms; virtually all patients who received prophylaxis were treated with cephalosporin. Simple cholecystectomies were carried out on 89% of patients and common duct explorations were performed on 11%. The average duration of surgery was 105 minutes. Eighteen per cent of wounds were not drained, 67% were drained through a stab wound, and 15% were drained through the incisional wound.

Microbiologic Findings

Overall, 13 of the 347 patients (3.8%) had wound infections. The rate was 1.9% for patients undergoing simple cholecystectomies and 18.4% for patients having examinations of the common duct. Fifteen bacterial isolates were recovered from the nine wound infections that were cultured: Enterobacter sp. and enterococci in three each; Klebsiella sp., Staphylococcus aureus, and other gram-positive bacteria in two each; and Pseudomonas aeruginosa, Citobacter freundii, and Escherichia coli in one each. Four wound infections were not cultured. Six of the nine infected wounds contained organisms that were resistant to the cephalosporin used for prophylaxis.

Risk factors that predisposed to wound infection in these patients were similar to those that have been described by others. Increased relative risks of infection of five times or greater were observed in patients who had undergone common duct explorations, had jaundice, had bactibilia (Table 1). Patients with bactibilia had a rate of postoperative infection that was almost six times that of patients with negative intraoperative bile cultures (p < 0.05). Bile cultures were positive in five of the nine patients who had cultures taken during a surgery and subsequently had infections. Thus, the sensitivity of bactibilia for identifying patients who later had infections was 56%; the specificity was 79%. The same species of bacteria were recovered from both specimens in only two of the five patients who had both bactibilia and infection.

Bactibilia was identified in 46 of the 245 intraoperative bile cultures (19%) that were available from surgery. Enteric bacteria predominated, with more than half of the isolates being E. coli or Klebsiella sp. Patients who had had prior biliary surgery, undergone common duct examinations, had fatal underlying diseases, and were older than 70 years had an increased rate of bactibilia (Table
2). Patients who had underlying debilitating diseases or were elderly frequently had had prior biliary disease and required common duct examinations. We did not observe a statistically significant association between acute cholecystitis, defined by clinical or histologic criteria, and either positive intraoperative bile cultures or postoperative infections. A strong association was noted between positive bile cultures and positive intraoperative wound cultures; 12 of 46 wound cultures (26%) were positive when bactibilia was present compared with four of 199 (2%) when bile cultures were negative (p < 0.001). Coagulase-negative staphylococci were recovered from eight of the 16 positive intraoperative wound cultures, and enteric bacteria were recovered from six. The same species of bacteria were recovered from both wound and bile cultures in only five of the 12 patients for whom both cultures were positive.

Bacteria were recovered from cultures of wound surfaces at surgery in 7% of cases (24 of the 347 cholecystectomies studied). There was a significant association between positive intraoperative wound cultures and subsequent infection; in 16.7% of patients with positive wound cultures at surgery postoperative infection developed, compared with 2.8% of patients with negative intraoperative wound cultures (p < .05). However, none of the organisms identified in the intraoperative wound cultures were recovered from the infections. There was no statistical association between other clinical risk factors that predisposed to infection and positive wound cultures.

High-risk patients generally received perioperative prophylaxis with cephalosporin antibiotics. No significant reduction in bactibilia, positive intraoperative wound cultures, or infection was noted in patients who received prophylaxis compared with those who did not. In fact, the rates of bactibilia and postoperative infection were higher in patients who had received prophylaxis than those who had not (22.2% vs. 10.1%, respectively, for bactibilia and 4.4% vs. 2.5%, respectively, for infection). However, antibiotics were not prescribed in a randomized fashion, and patients who received them were at greatest risk for bactibilia and infection. Ten of the 13 patients who had postoperative wound infections had received prophylactic antibiotics. All six patients who had infections with cephalosporin-resistant organisms had received prophylaxis; of the other four, one was infected with a sensitive organism and three did not have their infections cultured. Two of the three infected patients who had not received prophylaxis were infected with sensitive organisms; the other patient did not undergo culture.

**Discussion**

Before the introduction and widespread use of prophylactic antibiotics, wound infection rates after gallbladder surgery ranged from 10–20%. Prophylactic antibiotics have been effective in preventing postcholecystectomy wound infection in controlled clinical trials and in studies in which high-risk patients have been treated selectively (Fig. 1). When prophylactic antibiotics are used appropriately, infection rates are generally less than 6%. The overall rate of infection in the current study was 3.8%.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>No. of Patients</th>
<th>No. of Bactibilia</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior biliary surgery</td>
<td>4</td>
<td>4</td>
<td>100</td>
</tr>
<tr>
<td>Common duct exploration</td>
<td>33</td>
<td>17</td>
<td>52</td>
</tr>
<tr>
<td>Death</td>
<td>9</td>
<td>6</td>
<td>67</td>
</tr>
<tr>
<td>Age &gt;70 years</td>
<td>45</td>
<td>23</td>
<td>51</td>
</tr>
<tr>
<td>Acute cholecystitis</td>
<td>65</td>
<td>17</td>
<td>26</td>
</tr>
</tbody>
</table>

**Table 2. Risk Factors for Bactibilia**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>No. of Patients</th>
<th>Bactibilia</th>
<th>%</th>
<th>Relative Risk*</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior biliary surgery</td>
<td>241</td>
<td>42</td>
<td>17</td>
<td></td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Common duct exploration</td>
<td>212</td>
<td>29</td>
<td>14</td>
<td>6.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death</td>
<td>236</td>
<td>40</td>
<td>17</td>
<td>9.8</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Age &gt;70 years</td>
<td>200</td>
<td>23</td>
<td>12</td>
<td>8.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Acute cholecystitis</td>
<td>180</td>
<td>29</td>
<td>16</td>
<td>1.8</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = not significant.

* Number of times greater the risk of infection in patients with risk factors present.
Prophylactic antibiotics prevent infections even though they do not sterilize bile.\textsuperscript{16,23,25,27,28} (Fig. 2). Rates of bactibilia are not reduced by prophylactic antibiotics that achieve bile levels that exceed the minimum inhibitory concentrations of recovered bacteria.\textsuperscript{27,28} Yet, decreased rates of postoperative infection are invariably reported in patients who have received prophylaxis even when rates of bactibilia are similar in treated patients and untreated controls.\textsuperscript{16,17,23–28} Prophylactic antibiotics that achieve good tissue levels but subtherapeutic biliary levels are also effective in preventing postcholecystectomy wound infections.\textsuperscript{23} When used in the immediate preoperative period, prophylactic antibiotics do not select antibiotic-resistant organisms in bile. In our study, cephalosporin-sensitive \textit{E. coli} and \textit{Klebsiella} sp. were the most common organisms recovered from intraoperative bile cultures.

In studies in which patients have received no prophylactic antibiotics, a very strong association between bactibilia and infection was observed.\textsuperscript{1,3,6–8,14,15,21,22,23,26} The infection rate for patients with positive bile cultures has ranged from 20–60\% (Fig. 3). However, more recent studies involving patients who have received prophylaxis have not shown as high a positive predictive value for bile cultures. Even though bactibilia has remained an important epidemiologic predictor of infection, in most studies, infections develop in only 5–15\% of patients with positive bile cultures who received prophylaxis.\textsuperscript{12–14,16,22,23,27,28} In the current study, the rate was 11\%.

We had hypothesized that there would be a significant association between the recovery of bacteria from the bile during surgery, positive intraoperative wound cultures at closing, and subsequent infection. Indeed, this was the case. However, there was a poor correlation among the bacterial species recovered from the three sites. Antibiotic-
sensitive enteric bacteria were isolated from bile, skin flora and enteric bacteria were recovered from intraoperative wound cultures, and antibiotic-resistant enteric organisms were isolated from postoperative wound infections. In our study, six of the nine wound infections that were cultured contained bacterial species that were resistant to cephalosporins; each of these infections occurred in patients who had received prophylaxis with this class of antibiotic. In these patients, antibiotic-resistant organisms were isolated from infected wounds even though they were not recovered from intraoperative cultures of bile or the wound surface. Disparate results similar to those have been reported by others who have attempted to make similar correlations in gallbladder surgery or other procedures in which prophylactic antibiotics had been given. Postcholecystectomy wound infections with enterococci and *P. aeruginosa* have been reported by others in hospitals in which cephalosporins are used routinely for high-risk patients. These observations suggest that neither intraoperative cultures of bile or wound surfaces can be used to guide the choice of empiric therapeutic antibiotics when infection occurs in patients who have received prophylaxis.

The presence of bacteriuria continues to be a powerful epidemiologic marker to identify patients at high risk for postcholecystectomy wound infection. However, in patients who have received prophylactic antibiotics, it lacks the specificity, sensitivity, and direct clinical correlation to be used as the major criterion on which to base the choice of empiric therapeutic antibiotics for infection. The practice of obtaining routine cultures of bile during surgery from patients who have received prophylaxis now appears to be unnecessary and, at times, misleading. Bile cultures add additional cost to the patient's hospital stay without providing additional useful information to prevent infections or guide the choice of therapy.

**References**