Failure of Cefonicid Prophylaxis for Infectious Complications Related to Endoscopic Retrograde Cholangiopancreatography

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We performed a controlled study to evaluate the role of cefonicid in preventing infectious complications related to retrograde cholangiopancreatography (ERCP). Consecutive patients were randomized to receive prophylaxis with cefonicid (1 g intravenously) 1 hour before the procedure or to be untreated controls. During a 26-month period, 179 ERCPs, including 93 therapeutic procedures, were performed on 164 patients. Prophylaxis was administered before 88 procedures (49%). The rate of bacteremia among treated patients was similar to that among controls (3% vs. 2%, respectively; \( P = .4 \)). The rate of cholangitis was also similar among both groups (8% vs. 2%, respectively; \( P = .07 \)). There were no episodes of sepsis, and none of the patients died. The rate of bacteremia was also similar among patients undergoing diagnostic procedures and patients undergoing therapeutic procedures, but all cases of cholangitis occurred in the latter group (0 vs. 10%, respectively; \( P = .002 \)). Nevertheless, the rate of cholangitis was not significantly changed by the use of prophylaxis (14% among treated patients vs. 5% among controls, \( P = .12 \)). Therefore, infectious complications could not be prevented by cefonicid prophylaxis.

Infectious complications associated with endoscopic retrograde cholangiopancreatography (ERCP) are potentially serious causes of morbidity and mortality [1]. Although antibiotic prophylaxis is presently recommended for most patients undergoing this procedure, the optimal regimen, apparently, remains to be determined [2]. In this study, we evaluated the efficacy of cefonicid in the prevention of cholangitis and bacteremia following ERCP.

Patients and Methods

Patients were randomized either to receive cefonicid or to be untreated controls. Inclusion criteria included age of 18 years or older and written informed consent to participate in the study. Patients were excluded from the study if they presented with one of the following conditions: allergy to \( \beta \)-lactam antibiotics, sepsis, episodes of ascending cholangitis in the week before ERCP, or antibiotic therapy in the 72 hours before the procedure. By means of a computer-generated list, patients randomized to the prophylaxis group received cefonicid (1 g intravenously) 1 hour before the procedure. All procedures were performed by the same team of three experienced endoscopists. High-level disinfection of the endoscope was performed with full-strength 2% alkaline glutaraldehyde (Cidex, Johnson and Johnson Medical, Gargrave, UK) for 30 minutes. Blood for cultures was taken 5–10 minutes after the procedure and later whenever fever (temperature of \( \geq 38^\circ \text{C} \)) was present or sepsis was suspected.

This trial was approved by the hospital’s clinical experimentation committee. Cholangitis and sepsis were characterized according to previously reported definitions [3, 4]. Patients with abdominal pain and elevated levels of serum amylase following ERCP were considered to have pancreatitis. Symptomatic bacteremia was defined as a positive blood culture and fever (temperature of \( \geq 38^\circ \text{C} \)) or sepsis. Evaluations of all patients were continued for 7 days after each procedure. Outpatients were instructed to contact the endoscopist and/or return to the hospital whenever incipient signs of complications appeared. Data for the prophylaxis and control groups were compared by means of the Fisher’s exact test. A \( P \) value of <.05 was considered significant.

Results

Between March 1991 and May 1993, 179 ERCPs were performed on 164 patients. Prophylaxis was given before 88 procedures (49%). Both groups of patients were similar in terms of demographic and clinical characteristics. Of the 88 patients...
who received prophylaxis, three (3%) had bacteraemia and seven (8%) had cholangitis, findings similar to the rates among the control group (2% and 2%, respectively). No cases of sepsis were observed, and none of the patients died. Only one bacteraemic episode (occurring after a diagnostic ERCP) was symptomatic.

Of the 5 cases of bacteraemia, 3 were due to Escherichia coli, 1 was due to Klebsiella pneumoniae, and 1 was due to Shewanella (Pseudomonas) putrefaciens. The rate of bacteraemia was similar among patients undergoing diagnostic procedures and patients undergoing therapeutic procedures, but all nine episodes of cholangitis occurred in the latter group (0 vs. 10%, respectively; \( P = 0.002 \)). The rates of bacteraemia and cholangitis were also similar among cefonicid-treated patients who underwent therapeutic ERCPs and controls who underwent therapeutic ERCPs (2% vs. 5%, respectively \( P = 0.4 \); and 14% vs. 5%, respectively \( P = 0.12 \)). Of the nine episodes of cholangitis, five occurred in patients in whom obstruction of the common bile duct was not relieved. Four of these patients received prophylaxis. Of the four patients in whom cholangitis developed despite successful therapeutic ERCP, three received prophylaxis.

**Discussion**

Many aspects of antibiotic prophylaxis before ERCP remain debatable, mainly because of the paucity of controlled studies and some controversial results [2, 5]. It has been suggested that prophylaxis is probably not needed for low-risk patients; however, for those patients with biliary obstruction, antibiotic therapy not only is advisable but also should be continued until effective drainage is achieved [2, 6]. Although this approach can hardly be considered as "prophylactic," results of a recent randomized, double-blind, placebo-controlled study [3] may support it. In this trial, the rate of infectious complications following therapeutic ERCP was significantly reduced when piperacillin therapy was administered just before the procedure and was continued (up to 7 days) until the obstruction was completely relieved. Seven (22%) of the 32 patients receiving placebo had bacteraemia; these were the only cases of bacteraemia. The rate of clinical failure—defined as fever (temperature of \( >38.5^\circ \text{C} \)), cholangitis, and/or sepsis—was also significantly higher among the placebo group. However, data on the individual frequencies of cholangitis and sepsis following ERCP among both groups were not clearly provided.

Despite these convincing results, a word of caution should be sounded about the use of ureidopenicillins as prophylaxis for biliary tract infections because of the current high rate of resistance among many aerobic gram-negative organisms, particularly E. coli and Klebsiella [7]. Some authors have suggested the use of long-acting antibiotics as prophylaxis for infectious complications following ERCP [5]. Cefonicid was chosen as the prophylactic drug in our study because of its broad-spectrum activity against microbes, including most of the Enterobacteriaceae family, and because of its apparent efficacy as once-daily doses in preventing some postsurgical infectious complications [8].

Although we were unable to demonstrate any benefit from cefonicid prophylaxis for infectious complications associated with ERCP, the high incidence of cholangitis observed following therapeutic procedures appears to justify the use of antibiotic prophylaxis for high-risk patients. Further controlled trials of alternate prophylactic regimens for such patients are warranted.

**References**