Leading article

Endoscopic retrograde cholangiopancreatography and acute pancreatitis

Endoscopic retrograde cholangiopancreatography (ERCP) is firmly established as a valuable method for the diagnosis and treatment of biliary and pancreatic disease, and has a particularly important role in acute pancreatitis, when gall stones are suspected. Neoptolemos and colleagues' randomised patients thought to have gall stone pancreatitis to receive conservative management or urgent ERCP with sphincterotomy if stones were present in the bile duct. In patients with predicted mild disease on Glasgow criteria, urgent ERCP conferred no benefit, whereas it was associated with significantly lower morbidity in patients with predicted severe pancreatitis. None of the patients with mild disease in this trial died. There were fewer deaths in patients with severe disease who received urgent ERCP, although the difference was not statistically significant. A serum bilirubin concentration in excess of 40 μmol/l proved a strong indicator of 'persisting' bile duct stones and the need for ERCP. In a similar study from Hong Kong, early ERCP with sphincterotomy if stones were found reduced the incidence of biliary sepsis but did not affect mortality or the incidence of local and systemic complications.

In patients with acute pancreatitis of uncertain origin, ERCP may prove invaluable once the acute episode has settled to determine whether gall stones are present. The potential importance of 'biliary sludge' as a cause of acute pancreatitis has also been highlighted recently. Of 31 patients with idiopathic pancreatitis in one series, 23 (74%) had microscopic evidence of sludge (that is, calcium bilirubinate crystals or cholesterol monohydrate crystals) in duodenal aspirates. Pancreatitis recurred in only one of 10 patients undergoing cholecystectomy or endoscopic papillotomy compared with eight of 11 patients having no such treatment.

Early ERCP is probably unnecessary in patients with mild pancreatitis and should be avoided during the acute episode in patients without gall stones. Although the available results of early endoscopic intervention in patients with predicted severe gall stone pancreatitis are encouraging, some believe that the severity of an episode (and the risk of necrosis) is determined early, and that the amount of activated enzyme is more important than persisting impaction of a gall stone at the ampulla of Vater. If there is a 'window of opportunity' during which an episode of pancreatitis can be aborted by endoscopic sphincterotomy and stone extraction this window may be short-lived and have passed even before some patients reach hospital. Experimental necrotising pancreatitis in the opossum caused by obstructing the biliopancreatic duct system by a balloon catheter is less severe if the catheter is removed at one or three days compared with five days, lending support to the concept that early endoscopic removal of obstructing stones is beneficial in gall stone pancreatitis.

Despite its potential benefits, ERCP is not without risk in that it can actually cause acute pancreatitis, and result in significant morbidity and even mortality. Clinical acute pancreatitis occurs in some 1–5% of patients undergoing ERCP while asymptomatic hyperamylasaemia may be present in up to 50% of patients. In a referral centre treating 279 patients with acute pancreatitis over a five year period, ERCP was the causal factor in 4% of cases. While the overall death rate in the 279 patients in our review was 6%, three of 11 patients in the subgroup with ERCP related pancreatitis died, a death rate of 27%. Multiple or high pressure injections of contrast into the pancreatic duct, is a well recognised risk factor for ERCP related pancreatitis particularly when acinar filling of the pancreas is seen. Other risk factors include therapeutic endoscopic intervention, a past history of pancreatitis, and operator inexperience. The indication for ERCP may also be important and pancreatitis in one report was commoner when sphincter of Oddi dysfunction was being evaluated than when ERCP was being performed because of other indications, particularly gall stones.

Of the four patients who died in a series of 14 patients developing acute pancreatitis after ERCP, all showed a rising serum bilirubin concentration in the first 48 hours after the procedure. There was no such rise in those who survived. The lethal combination of ERCP related pancreatitis and subsequent deterioration in liver function could not be accounted for by the explanatory variables of age, sex, presence of choledocholithiasis at the time of ERCP, successful duct clearance, inadvertent production of a pancreatogram or the pre-ERCP serum bilirubin concentration when examined in a logistic regression model. The number of patients in this analysis is small so that the significance of a rising serum bilirubin after ERCP...
needs confirmation in a larger study. It could just reflect the persistence of biliary obstruction from continuing stone impaction in some cases, or oedema and muscle spasm of the sphincter of Oddi after endoscopic manipulation in others. Perhaps, concomitant obstruction of the pancreatic duct is more important in the pathophysiology of acute pancreatitis in exacerbating the severity of the disease. All four patients who died developed local pancreatic complications. Indeed, pancreatic duct obstruction or ligation is a recognised method of inducing pancreatitis in animal models. Sepsis, and cholangitis in particular, could also account for the rise in serum bilirubin concentration. Bilbao and coworkers in an early appraisal of the risks of ERCP considered that eight of 15 deaths in their review resulted from sepsis in an obstructed biliary system, although most of these patients had ducts that were obstructed by tumour rather than calculi. It may be that the serum bilirubin concentration is simply a non-specific marker of progression to severe disease with the development of a systemic inflammatory response and multiple organ failure, the common pathway to death in patients with lethal pancreatitis. What is not clear from our own retrospective study is whether early duct decompression in the four patients who died would have changed the clinical outcome.

Measures to prevent ERCP related pancreatitis are vital given its potential risks. Awareness and avoidance of known risk factors at the time of ERCP are important and the decision to proceed to ERCP should not be taken lightly. Meanwhile, research continues into agents that might prevent the development of ERCP related acute pancreatitis. Antibiotic prophylaxis, or the administration of glucagon or somatostatin have failed to achieve a significant reduction in the incidence of ERCP related pancreatitis, while the use of low osmolality contrast medium does not seem to confer any benefit. A multicentre Italian study randomised 424 patients to receive either gabexate mesilate (a synthetic protease inhibitor active against a broad spectrum of pancreatic proteases) or placebo by continuous intravenous infusion commencing 30 to 90 minutes before the ERCP and continuing for 12 hours thereafter. They showed a significant reduction in ERCP related acute pancreatitis from 9% (19 patients) in the control group to 1-4% (3 patients) in the treatment group.

In conclusion, early ERCP in patients with predicted severe acute gall stone pancreatitis is of benefit. However, the optimum timing of the procedure and the role of ERCP in non-gall stone pancreatitis requires further study. Pancreatitis after ERCP remains a potentially serious complication, and continuing biliary obstruction and cholangitis may compound the risk. While agents such as gabexate mesilate may prove useful in reducing the incidence of ERCP related pancreatitis, careful assessment of each patient with regard to the need for ERCP and attention to detail to minimise risk factors will certainly help to prevent this form of pancreatitis.

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Gut 1996 38: 799-800
doi: 10.1136/gut.38.6.799

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