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Sphincter of Oddi and Acute Pancreatitis: A New Treatment Option

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Acute pancreatitis is a disease with heterogeneous etiologies and an obscure pathogenesis. Gallstones, alcohol, hyperlipidemia, hypercalcemia, drugs or toxins, endoscopic retrograde cholangiopancreatography (ERCP), trauma, pancreatic cancer and sphincter of Oddi (SO) dysfunction are the well known causes of acute pancreatitis, but, in about 10-30% of patients, the disease is still categorized as idiopathic [1, 2]. Inasmuch as acute pancreatitis is often a once-only disease, invasive procedures such as ERCP, SO manometry or bile analysis are not routinely performed in all patients at the first attack. Acute pancreatitis is usually associated with small stone impaction in the common channel of the biliary and pancreatic ducts, and it is sometimes difficult to detect by image studies such as sonography, computed tomography or ERCP [3]. Lee *et al.* have reported that 74% of patients with so-called "idiopathic pancreatitis" had microscopic crystals in the bile [4]. The small stones or microscopic crystals can pass through the SO into the duodenum under normal condition, but these stones (crystals) may obstruct the common channel and induce bile reflux into the pancreatic duct if the SO fails to completely relax. In addition, the repeated passage of small stones through the common channel may lead to inflammation and fibrosis of the sphincter. A malfunctioning SO may allow chronic reflux of the duodenal juice into the pancreatic duct resulting in damage to the pancreas [2]. Alcohol is another common cause of acute pancreatitis. The pathogenesis of alcohol-related acute pancreatitis includes the direct deleterious effect of alcohol on pancreatic acinar cells and the induction of ampullitis or spasm of the SO [1, 2, 5]. Therefore, it is possible that SO dysfunction plays an important role in acute pancreatitis.

SO dysfunction can be diagnosed by typical symptoms and signs (i.e. biliary pain, abnormal biochemical tests and biliary dilatation), fatty meal sonography, cholescintigraphy and manometry [6, 7]. In the presence of other organic lesions such as stones or tumors, manometry is the only accurate test and is "the gold standard" for evaluating the SO function. Toouli *et al.* performed endoscopic or intraoperative manometry in 33 patients with recurrent pancreatitis. Stenosis of the SO was found in 24 patients and dyskinesia of the SO was found in six [8]. In contrast, Venu *et al.* studied 116 patients with idiopathic recurrent pancreatitis with the use of ERCP and manometry. Seventeen patients (14.6%) had SO dysfunction and 27 patients had an anatomical or organic lesion in the pancreaticobiliary tract. SO manometry was performed at least six weeks after the attack of acute pancreatitis in this study and the results may not be the same as those present during the acute attack [9]. We performed SO manometry in 18 patients with acute alcoholic pancreatitis and in two patients with idiopathic pancreatitis within one week after admission. SO dysfunction was diagnosed in 14 patients (70%). In 6 of the 14 patients, the diagnosis of stenosis was made without the aid of manometry as the sphincter was too

tight to allow the insertion of a manometric catheter. Seven patients had SO basal pressure greater than 40 mmHg and one patient with idiopathic pancreatitis had a paradoxical reaction to somatostatin infusion [10]. This study suggests that SO dysfunction is a common finding present in patients with alcoholic pancreatitis. SO spasms resulting in gallstone pancreatitis was first postulated in 1913 [11, 12]. Toouli *et al.* have reported an increase of retrograde propagation of SO contractions in patients with common bile duct stones [13]. Endoscopic sphincterotomy and balloon dilatation are widely used to retrieve bile duct stones despite sphincteric function. Recurrent biliary complications including cholangitis and bile duct stones may occur after long-term follow-up, but recurrent pancreatitis after sphincteric ablation is rare [14, 15].

SO manometry is not routinely performed in patients having their first attack of acute pancreatitis because of its technical difficulty and potential complications such as postprocedural pancreatitis. It is uncertain whether the change in SO function in those patients having a first attack of non-biliary pancreatitis is a transient abnormality due to acute inflammation or a permanent event. Division of the SO by endoscopic sphincterotomy is helpful in prevention of recurrent attacks in patients with SO stenosis [8], but it is possible that pharmacological treatment to relax the hypertensive sphincter may be enough in some patients with idiopathic pancreatitis. Furthermore, detailed studies including ERCP, bile analysis and SO manometry should be conducted in patients with so-called "idiopathic pancreatitis" because more than 70% of those patients were found to have underlying causes such as microlithiasis, SO dysfunction, and pancreas divisum [16, 17, 18].

Somatostatin is a potent inhibitor of pancreatic enzyme secretions and has been used in the treatment of acute pancreatitis. Although some studies have demonstrated the stimulating effect of SO activity by a long-acting somatostatin analogue (octreotide [19]), the native hormone, somatostatin-14 has been shown to inhibit SO activity [20]. Somatostatin can reduce SO basal pressure significantly in more than 93% of patients with non-biliary pancreatitis [10], and most of those on continuous infusion of somatostatin felt well even after pancreatic cannulation during SO manometry. Besides relaxation of the SO, somatostatin also has the effects of inhibition of pancreatic secretion, stimulation of the reticuloendothelial system, prevention of endotoxemia and cytoprotection, and it may be the drug of choice to alleviate the symptoms and reduce the complications of acute pancreatitis, especially after an ERCP procedure. The drawbacks of somatostatin include its high cost, short acting effect, impairment of the gallbladder or biliary emptying and paradoxical response in some patients.

In conclusion, SO dysfunction is underestimated in patients with acute pancreatitis because most of these patients do not undergo manometric studies before definite treatment such as sphincterotomy. SO relaxants, such as somatostatin, may be beneficial in some patients with acute non-biliary pancreatitis especially in preventing post-ERCP or post-SO manometry complications, but additional controlled studies are needed to confirm their effects.

Key words Oddi's Sphincter (abnormalities, injuries; physiopathology; pathology) Manometry; Pancreatitis (etiology, drug therapy); Pancreatitis, Acute Necrotizing; Pancreatitis, Alcoholic; Somatostatin

Abbreviations ERCP: endoscopic retrograde cholangiopancreatography; SO: sphincter of Oddi

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