Effect of somatostatin on the sphincter of Oddi in patients with acute non-biliary pancreatitis

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Abstract

Background—Somatostatin has been used to prevent pancreatitis after endoscopic retrograde cholangiopancreatography but its effect on acute non-biliary pancreatitis is still unclear.

Aim—The purpose of this study was to evaluate the function of the sphincter of Oddi (SO) and the effect of somatostatin on patients with non-biliary pancreatitis.

Methods—Twenty patients (18 males, two females) with acute pancreatitis (alcoholic 18, idiopathic two) received SO manometry within one week after admission. After baseline measurement, a bolus dose of somatostatin (Stilamin, Serono) 250 µg was infused slowly, and SO manometry was repeated after five minutes. Continuous infusion of somatostatin 250 µg/h was given for 12 hours after SO manometry. Serum amylase, lipase, glucose, and C reactive protein (CRP) levels were examined before and after somatostatin infusion.

Results—SO manometry was unsuccessful in six patients due to contracted sphincter. In the remaining 14 patients, high SO basal pressure (SOBP >40 mm Hg) was found in seven patients. After somatostatin infusion, mean SOBP decreased from 48.8 (29) to 31.9 (22) mm Hg (p<0.01). One patient had a paradoxical reaction to somatostatin (SOBP increased from 30 to 50 mm Hg) while the other 13 patients had a fall in SOBP after somatostatin. One patient developed abdominal pain with a serum amylase level of 2516 IU/l after SO manometry. No other side effects or changes in amylase, lipase, glucose, or CRP levels were observed in the other 19 patients after SO manometry and somatostatin infusion.

Discussion—Sphincter of Oddi dysfunction is common in patients with acute non-biliary pancreatitis and in most cases somatostatin can relax the sphincter.

Keywords: acute alcoholic pancreatitis; sphincter of Oddi; somatostatin

Abbreviations used in this paper: SO, sphincter of Oddi; CRP, C reactive protein; SOBP, SO basal pressure; CBD, common bile duct.
position of the catheter. The catheter was considered in the pancreatic duct if no bile stained fluid was aspirated. Pressure was measured first in the pancreatic duct, and then in the SO and duodenum using the station pull through technique. After baseline measurements for three minutes, somatostatin 250 µg (Stilamin, Serono, Switzerland) was infused intravenously over three minutes. SO manometry was repeated five minutes after somatostatin infusion. After SO manometry, continuous infusion of somatostatin at a rate of 250 µg/h for 12 hours was started. Basal SO pressure >40 mm Hg was defined as SO dysfunction. Serum amylase, lipase, glucose, and C reactive protein (CRP) levels were measured before and 12 hours after SO manometry.

The human research committee of Kaohsiung Veterans General Hospital approved the study. The protocol was explained to each patient and written consent was obtained. A paired t test was used to compare values before and after somatostatin infusion in the same patient. Values of p<0.05 were considered significant.

Results
Patient characteristics are shown in table 1. There were 18 males and two females, aged 26–61 years. Eleven patients had a high serum cholesterol (> 200 mg%) or triglyceride (>200 mg%) level. Ten patients had fever on admission but the fever subsided with conservative treatment before SO manometry. Pancreatitis was graded according to the computed tomography criteria of Balthazar and colleagues: 12 patients had grade C, four patients grade D, and four patients grade E.

SO manometry was successfully performed in 14 of 20 patients (70%). Deep cannulation of the catheter failed in six patients (all male, mean age 39.7 years, grade C in two patients, grade D in three patients, and grade E in one patient) due to a contracted sphincter. There were no significant differences in age, sex, grading, serum amylase, lipase, glucose, or CRP between the six patients with failed cannulation and the 14 patients with successful cannulation. In 14 patients with successful SO manometry, cannulation of the pancreatic duct was confirmed by the absence of bile from the catheter after deep insertion.

The results of SO manometry in 14 patients are shown in table 2. SOBP was higher than 40 mm Hg in seven patients with alcoholic pancreatitis and three had tonic contraction. After somatostatin infusion, 13 patients had a significant fall in SOBP and one patient with idiopathic pancreatitis had a paradoxical reaction (SOBP rose from 30 to 50 mm Hg after somatostatin infusion) (figs 1, 2). Mean SOBPs in 14 patients before and after somatostatin infusions were 48.8 (29) mm Hg and 31.9 (22) mm Hg, respectively (p<0.01). One patient with grade E alcoholic pancreatitis and an SOBP of 110 mm Hg developed severe abdominal pain and marked elevation of serum enzymes.

### Table 1 Patient characteristics

<table>
<thead>
<tr>
<th>n</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>18/2</td>
</tr>
<tr>
<td>Age (y) (mean (range))</td>
<td>41.7 (27–61)</td>
</tr>
<tr>
<td>Alcoholic abuse</td>
<td>18</td>
</tr>
<tr>
<td>Serum cholesterol &gt;200 mg%</td>
<td>9</td>
</tr>
<tr>
<td>Serum triglyceride &gt;200 mg%</td>
<td>9</td>
</tr>
<tr>
<td>CT grading (C/D/E)</td>
<td>12/4/4</td>
</tr>
</tbody>
</table>

CT, computed tomography.

### Table 2 Age, sex, computed tomography (CT) grade, and sphincter of Oddi basal pressure (SOBP) in the 14 patients with acute non-biliary pancreatitis

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Age (y)</th>
<th>Sex</th>
<th>CT grade</th>
<th>SOBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>Male</td>
<td>C</td>
<td>74</td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>Male</td>
<td>C</td>
<td>20</td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>Male</td>
<td>C</td>
<td>38</td>
</tr>
<tr>
<td>4</td>
<td>52</td>
<td>Male</td>
<td>C</td>
<td>70</td>
</tr>
<tr>
<td>5</td>
<td>35</td>
<td>Male</td>
<td>C</td>
<td>95</td>
</tr>
<tr>
<td>6</td>
<td>43</td>
<td>Male</td>
<td>C</td>
<td>50</td>
</tr>
<tr>
<td>7</td>
<td>30</td>
<td>Male</td>
<td>C</td>
<td>20</td>
</tr>
<tr>
<td>8</td>
<td>50</td>
<td>Female</td>
<td>C</td>
<td>10</td>
</tr>
<tr>
<td>9</td>
<td>54</td>
<td>Male</td>
<td>C</td>
<td>70</td>
</tr>
<tr>
<td>10</td>
<td>35</td>
<td>Male</td>
<td>C</td>
<td>10</td>
</tr>
<tr>
<td>11</td>
<td>61</td>
<td>Female</td>
<td>D</td>
<td>30</td>
</tr>
<tr>
<td>12</td>
<td>30</td>
<td>Male</td>
<td>E</td>
<td>36</td>
</tr>
<tr>
<td>13</td>
<td>36</td>
<td>Male</td>
<td>E</td>
<td>50</td>
</tr>
<tr>
<td>14</td>
<td>54</td>
<td>Male</td>
<td>E</td>
<td>110</td>
</tr>
</tbody>
</table>

Figure 1 Sphincter of Oddi manometry in patient No 5 before and after somatostatin infusion.

Figure 2 Sphincter of Oddi (SO) basal pressure before and after somatostatin infusion in 14 patients with acute non-biliary pancreatitis.
somatostatin in non-biliary pancreatitis

Discussion

Although SO dysfunction is generally thought to be a cause of acute pancreatitis, the incidence of SO dysfunction in acute pancreatitis is unknown. The gold standard in evaluation of SO function is SO manometry but it is not routinely used as a diagnostic test for acute pancreatitis due to technical difficulties and the potential complications, particularly postprocedural pancreatitis.

Cuschieri et al found eight patients with gall stone pancreatitis whose basal pressures of SO were lower than normal. However, Guerud et al demonstrated that patients with common bile duct (CBD) stones and recurrent pancreatitis had higher SOBPs than control subjects or patients with CBD stones and no history of pancreatitis. Basal SO pressures in patients with alcoholic pancreatitis were also different in previous studies. From the results of lowering of SOBP by intravenous and intragastric instillation of alcohol, Vicente speculated that alcohol could predispose to the development of pancreatitis by allowing pancreaticoduodenal reflux to occur. Goff reported a non-significant fall in mean basal pancreatic duct sphincter pressure and a significant fall in phasic contraction and mean amplitude after infusion of 80 g of whisky into the stomach. However, basal SO pressures in patients with pancreatitis before alcohol infusion were higher than non-pancreatitis patients. In contrast, Guerud et al observed tonic SO contraction after local instillation of high concentrated (40%) alcohol solution in patients with alcoholic pancreatitis. Tarnasky et al also reported that patients with SO dysfunction were four times more likely to have evidence of chronic pancreatitis than those without SO dysfunction.

In our study, 50% of patients with acute non-biliary pancreatitis had high SOBP. If we include the six patients with spastic SO during manometry as abnormal, 13/18 patients (73%) with acute alcoholic pancreatitis had abnormal SO function. The difference in SO function in our patients with alcoholic pancreatitis from that in previous studies may be due to differences in the methods used. Most patients are reluctant to undergo SO manometry during the acute stage of pancreatitis because it is a relatively painful procedure. The timing of SO manometry was not the same in previous studies and some patients underwent SO manometry after the acute inflammation subsided. In addition, isolated elevation of basal pressure of the pancreatic SO or biliary SO may occur independently. Selective cannulation of the pancreatic duct for manometry is important in patients with acute pancreatitis.

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 octreotide, a long acting somatostatin analogue, on SO activity, the native hormone, somatostatin-14, has been shown to inhibit SO activity in several studies. In our study, somatostatin reduced SOBP significantly in more than 93% of patients, and most of those on continuous infusion of somatostatin felt well even after pancreatic cannulation during SO manometry. Somatostatin relaxes the SO allowing free drainage of pancreatic secretions and it may be the drug of choice to alleviate symptoms and reduce the complications of endoscopic retrograde cholangiopancreatography in patients with acute pancreatitis. The drawbacks of somatostatin include its short acting effect and paradoxical response in some patients. Reflex of duodenal juice after SO relaxation or sphincterotomy rarely occurs.

In conclusion, SO dysfunction is commonly present in patients with acute alcoholic pancreatitis. Somatostatin can relax the SO and may be a useful drug in acute alcoholic pancreatitis.

Table 3 Serum amylase, lipase, fasting glucose, and C reactive protein (CRP) levels before and after sphincter of Oddi manometry (SOM)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>After SOM</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylase (U/l)</td>
<td>397 (120)*</td>
<td>340 (130)</td>
</tr>
<tr>
<td>Lipase (U/l)</td>
<td>800 (721)</td>
<td>657 (584)</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>156 (10)</td>
<td>153 (21)</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>11.1 (4.3)</td>
<td>8.8 (5.8)</td>
</tr>
</tbody>
</table>

Values are mean (SEM).

amylose to 2516 IU/l (normal <160 IU/l) after SO manometry but symptoms subsided after two weeks of conservative treatment. No additional side effects were found in the other 19 patients. There were no significant differences in mean serum amylase, lipase, glucose, or CRP levels in the 20 patients before and after SO manometry and somatostatin infusion (table 3).

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