Clinical and scintigraphic assessment of the role of endoscopic sphincterotomy in the treatment of sphincter of Oddi dysfunction

G M Fullarton, T Hilditch, A Campbell, W R Murray

Abstract
Postcholecystectomy pain caused by sphincter of Oddi dysfunction remains a difficult condition to treat. Endoscopic sphincterotomy has been recommended for those patients with confirmed sphincter of Oddi motor abnormalities. We have studied sphincter of Oddi dysfunction patients to evaluate the effects of endoscopic sphincterotomy on both clinical symptoms and previously reported scintigraphic parameters to determine the efficacy of this method of treatment. Nine postcholecystectomy patients (seven women, two men, median age 59 years) with clinical and manometric evidence of sphincter of Oddi dysfunction underwent endoscopic sphincterotomy for persisting biliary type pain. Each patient had scintigraphy before and eight weeks after endoscopic sphincterotomy. The patients symptomatic response was assessed independently at three monthly intervals after endoscopic sphincterotomy. Scintigraphic analysis showed that the TMAX (time to maximum counts) was significantly reduced from 25-0 (20-36) (median [range]) before endoscopic sphincterotomy to 15-0 (13-25) after endoscopic sphincterotomy (p<0.01). Seven of nine (78%) sphincter of Oddi dysfunction patients had significant improvement in their symptoms after a mean follow up period of 12 months (range 6-19) although only six of nine were totally pain free. These results suggest that endoscopic sphincterotomy in manometrically confirmed sphincter of Oddi dysfunction improves bile drainage as measured by quantitative cholescintigraphy and is associated with at least short-term symptom relief in the majority of patients.

Sphincter of Oddi dysfunction is a recognised cause of postcholecystectomy pain in 9-14% of cases, although its true prevalence remains unclear. It is, however, a difficult condition to diagnose requiring endoscopic biliary manometry to confirm sphincter pressure abnormalities. We have recently reported that quantitative cholescintigraphy using 99mTc-DISIDA can detect alterations in labelled bile flow in postcholecystectomy patients with manometric evidence of sphincter of Oddi dysfunction. In these patients endoscopic sphincterotomy has been recommended as the treatment of choice although few clear therapeutic guidelines exist at present. In addition cholescintigraphy may provide a simple non-invasive method to quantify the effects of endoscopic sphincterotomy on biliary dynamics.

The aim of this study was therefore to examine the effects of endoscopic sphincterotomy on symptoms and scintigraphic parameters in postcholecystectomy patients with manometric evidence of sphincter of Oddi dysfunction to determine the efficacy of this method of treatment.

Methods
PATIENTS
Nine postcholecystectomy patients (seven women, two men) with a median age of 59 years (range 35-74) presented with clinically suspected sphincter of Oddi dysfunction (recurrent biliary type pain transient liver function test changes dilated common bile duct at ERCP) and all underwent endoscopic biliary manometry to confirm sphincter motor abnormalities. Eight patients had transient abnormalities in either transaminases and/or alkaline phosphatase associated with attacks of pain (Table I) although these subsequently all returned to normal. All nine study patients had a dilated common bile duct (≥12 mm) at time of ERCP (Table I). Patients presented at a median time interval of five years (range eight months-26 years) after cholecystectomy with a median symptom free interval after surgery of two years (range three months-22 years).

**TABLE I**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>Sex</th>
<th>AST (U/l)</th>
<th>ALT (U/l)</th>
<th>ALP (U/l)</th>
<th>CBD diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MN</td>
<td>56</td>
<td>F</td>
<td>54</td>
<td>35</td>
<td>200</td>
<td>15</td>
</tr>
<tr>
<td>JS</td>
<td>74</td>
<td>F</td>
<td>32</td>
<td>40</td>
<td>158</td>
<td>15</td>
</tr>
<tr>
<td>EB</td>
<td>59</td>
<td>F</td>
<td>200</td>
<td>200</td>
<td>250</td>
<td>13</td>
</tr>
<tr>
<td>AR</td>
<td>53</td>
<td>F</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>12</td>
</tr>
<tr>
<td>AM</td>
<td>73</td>
<td>M</td>
<td>17</td>
<td>29</td>
<td>196</td>
<td>16</td>
</tr>
<tr>
<td>JM</td>
<td>71</td>
<td>M</td>
<td>143</td>
<td>152</td>
<td>154</td>
<td>12</td>
</tr>
<tr>
<td>MF</td>
<td>35</td>
<td>F</td>
<td>58</td>
<td>61</td>
<td>67</td>
<td>13</td>
</tr>
<tr>
<td>EM</td>
<td>60</td>
<td>F</td>
<td>52</td>
<td>197</td>
<td>312</td>
<td>15</td>
</tr>
<tr>
<td>RM</td>
<td>59</td>
<td>F</td>
<td>86</td>
<td>170</td>
<td>228</td>
<td>16</td>
</tr>
</tbody>
</table>

Normal range AST (10-35), ALT (10-50), ALP (35-130). AST = aspartate aminotransferase; ALT = alanine aminotransferase, ALP = alkaline phosphatase; CBD = common bile duct; LFT = liver function tests; N = normal value.

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equipment gave a postocclusion pressure rise rate of 450 mmHg/s. Polyethylene triple lumen catheters were used (Arndorfer Medical Specialties Inc, Greendale, Wisconsin, USA) with an outer diameter of 1.7 mm and inner luminal diameter of 0.5 mm. Each catheter had three side holes 2 mm apart, the most distal hole being 5 mm from the catheter tip. Catheters had eight black rings 1 mm wide at 2 mm intervals to determine the depth of insertion of the catheter into the sphincter of Oddi.

Biliary manometry was performed in the fasting state at time of ERCP under diazepam sedation only (5–10 mg iv). No analgesia or smooth muscle relaxants were used. With the patient prone a station pull through technique was used to measure active sphincter segment pressures simultaneously for at least two minutes with duodenal pressure referenced as zero. The catheters position in the bile duct was confirmed by contrast injection after manometry. Sphincter basal pressure was calculated as the mean pressure at base of phasic contractions over a two minute recording period. Phasic wave amplitude was calculated as the mean pressure rise above basal pressure over the two minute recording period.

**MANOMETRIC CONTROL GROUP**

Our manometric control group consisted of 18 patients (16 women, two men, median age 49 years, range 27–92). In this group of patients 12 had common bile duct stones (all postcholecystectomy and six had no evidence of pancreaticobiliary disease. These six patients had all been extensively investigated for relatively minor upper gastrointestinal complaints with no abnormality being detected in the gastrointestinal tract. Their symptoms were attributed to irritable bowel syndrome in five, one patient was subsequently found to have porphyria. Previous manometric studies have validated the use of patients with common bile duct stones as control subjects.11 Using our manometry control data we considered sphincter of Oddi dysfunction to be present if sphincter of Oddi mean basal pressure and/or phasic pressure exceeded the mean control values by >2 SD (Table II). All nine study patients had manometric evidence of sphincter of Oddi dysfunction based on this criteria.

**STUDY PROTOCOL**

These nine patients with clinical and manometric evidence of sphincter of Oddi dysfunction were then entered into the study. All were clinically well at time of study and routine liver function tests (serum bilirubin, alkaline phosphatase, and transaminases) were normal in all subjects before cholecintigraphy.

**TABLE II: Sphincter of Oddi pressures in dysfunction group**

<table>
<thead>
<tr>
<th></th>
<th>Basal (mmHg)</th>
<th>Phasic (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SO dysfunction (n=9)</td>
<td>26 (9-22-42)</td>
<td>141 (0-112-224)</td>
</tr>
<tr>
<td>Controls (n=18)</td>
<td>14 (0-22-3)</td>
<td>82.5 (54-102)(110)</td>
</tr>
</tbody>
</table>

Median (ranges). Figures in parentheses indicate our upper limit of normal based on control means ± 2 SD.

Each patient underwent cholecintigraphy with 99mTc-DISIDA before and eight weeks after endoscopic sphincterotomy. Endoscopic sphincterotomy was performed in all patients by a single operator (WRM) using a traction type papillotomy knife (Olympus Corp, Tokyo, Japan) dividing the sphincter from the ampullary orifice to the transverse duodenal mucosal fold.12 Using this technique we demonstrated ablation of sphincter of Oddi basal pressure with zero pressure gradient between the duodenum and common bile duct in the first four patients treated (MN, EM, IS, AM). Each patients symptom status was assessed by an independent observer at three monthly intervals after endoscopic sphincterotomy.

**SCINTIGRAPHIC TECHNIQUE**

After an overnight fast 150-MBq of 99mTc-DISIDA (Hepatolite, Dupont UK, Ltd) were given at time zero. Imaging was carried out using a large field gamma camera (Siemens ZLC 750) interfaced to a computer (Nodecrest Limited). Data were recorded with the subject supine under the gamma camera as a continuous series of 60 frames each of one minute duration and stored on computer disk for later analysis.

Regions of interest were drawn around the entire hepatobiliary system (liver and extrahepatic bile ducts) and activity/time curves created by computer analysis for this region of interest after correction for radioactive decay. The common bile duct was also outlined as a separate region of interest, however, this was often technically difficult because of duodenal overlap. In addition preliminary analysis of this region of interest produced similar results to those of the entire hepatobiliary system. The simpler hepatobiliary region of interest was therefore used through the study. Results for this hepatobiliary region of interest were expressed as (Fig I): (1) TMAX (Time in minutes from zero to maximum counts) reflecting hepatic uptake and early biliary clearance. (2) E45 (%) (biliary emptying at 45 minutes) – that is, activity cleared at 45 minutes as a percentage of the maximum counts in the region of interest. (3) E60 (%) (biliary emptying at 60 minutes) – that is, activity cleared at 60 minutes as a percentage of the maximum counts in the region of interest.

Analysis was performed by staff unaware of the patients clinical condition. Statistical analysis was performed using paired Wilcoxon’s rank-sum test (2 sided) and significance was taken at the 5% level (p<0.05).

**Results**

**SCINTIGRAPHY**

Results for TMAX, E45 and E60 before and after endoscopic sphincterotomy are shown in Table III.

TMAX values decreased in eight of nine patients after endoscopic sphincterotomy (p<0.01) and remained unchanged in one patient (Fig 2). E45 was also significantly increased after sphincterotomy in seven of nine patients (p<0.05).
The effect of endoscopic sphincterotomy on quantitative biliary dynamics is best seen in the activity/time curves from a representative sphincter of Oddi dysfunction patient (Fig 3).

CLINICAL RESPONSE

Patients have been assessed at a median time period of 12 months (range 6–19) after endoscopic sphincterotomy. Seven of nine (78%) patients were symptomatically improved after endoscopic sphincterotomy although only six were totally asymptomatic at time of review (Table IV). Two patients (EM, RM) had unchanged symptoms after sphincterotomy despite improvement in their scintigraphic parameters (Fig 2) and confirmation of sphincter of Oddi ablation by repeat endoscopic biliary manometry. The two patients (EM, RM) who failed to respond to endoscopic sphincterotomy have both since been extensively investigated by barium series, upper and lower gastrointestinal endoscopy, abdominal ultrasound and 24 hour oesophageal pH monitoring. This has resulted in possible alternative diagnoses in both patients (EM – diverticular disease, RM – gastro-oesophageal reflux). Overall therefore endoscopic sphincterotomy was beneficial in seven of nine (78%) patients with only two of nine (22%) patients demonstrating no symptom improvement. Patient 3 (EB) developed recurrent symptoms 12 months after endoscopic sphincterotomy and had manometrically confirmed sphincter restenosis (basal pressure 58 mmHg, phasic pressure 116 mmHg). Repeat 99mTc-DISIDA scan at this time revealed a TMAX of 31 minutes compared with 20 minutes after sphincterotomy. A further endoscopic sphincterotomy was performed and repeat scintigraphy eight weeks later showed a reduction in TMAX to 15 minutes (within our normal range). The patient remains significantly improved up to three months following this second sphincterotomy.

Discussion

This study has shown that in postcholecystectomy patients with manometric evidence of sphincter of Oddi dysfunction, endoscopic sphincterotomy improves bile drainage as measured indirectly by quantitative cholescintigraphy and is associated with at least short term symptom relief in the majority of patients.

The introduction of endoscopic biliary manometry has been associated with increased recognition of sphincter of Oddi dysfunction as a cause of postcholecystectomy pain in patients with no demonstrable pancreaticobiliary abnormalities using conventional imaging techniques. 3, 11, 13, 18, 23

The term sphincter of Oddi dysfunction has been used to encompass all identifiable manometric disorders including both fixed fibrotic sphincter of Oddi stenosis and true motor dysfunction. Although the pathogenesis of this condition is unclear cholecystectomy may predispose to sphincter of Oddi dysfunction either through direct sphincter trauma 26 (leading to
Before Figure 2: TMAX values before and eight weeks after endoscopic sphincterotomy (ES) in nine patients with manometrically confirmed sphincter of Oddi dysfunction. The two patients (EM and RM) who had continuing symptoms post-ES are indicated by hatched lines.

After

Figure 3: Representative activity/time curves in a sphincter of Oddi dysfunction patient before and 8 weeks after endoscopic sphincterotomy (ES) showing changes in quantitative biliary dynamics.
TABLE IV Clinical response after endoscopic sphincterotomy

<table>
<thead>
<tr>
<th>Subject</th>
<th>Time post endoscopic sphincterotomy (months)</th>
<th>Asymptomatic Improvement</th>
<th>No better/no improvement</th>
<th>More severe symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) MN</td>
<td>19</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2) IS</td>
<td>14</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>3) EB</td>
<td>12</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>4) AB</td>
<td>11</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>5) AM</td>
<td>7</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>6) JM</td>
<td>6</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>7) MF</td>
<td>14</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>8) EM</td>
<td>15</td>
<td>+</td>
<td>+</td>
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</tr>
<tr>
<td>9) RM</td>
<td>12</td>
<td>+</td>
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