

Chapter 23

**Endotherapy of chronic pancreatitis –
the Indian experience**

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Summary

Endotherapy remains an important therapeutic modality in the management of chronic calcific (tropical) pancreatitis. It offers a viable alternative to surgery and can be repeated with minimal morbidity. However, Endotherapy is not always an alternative to surgery although it is hoped that by early endoscopic and medical intervention, the subsequent need for surgery is at best delayed or not obviated.

Introduction

Chronic pancreatitis is a relentless disease with no curative treatment. The goals of therapy are palliative and possibly to delay progression of the disease¹. The aims of palliative therapy are to alleviate pain, prevent attacks of pancreatitis, reduce pancreatic exocrine insufficiency and to possibly improve endocrine insufficiency. The role of lifestyle modification (alcohol and smoking cessation) must be emphasized to the patient.

The diagnosis of advanced chronic pancreatitis is clear with a typical history of recurrent persistent epigastric pain and radiological evidence of pancreatic calcification. In the absence of radio-opaque calcified calculi, endoscopic retrograde cholangiopancreatography (ERCP) is the next logical step. ERCP allows for detailed study of the main pancreatic duct and side branches thus assisting in both the diagnosis and planning of endoscopic or surgical therapy. With developments in magnetic resonance cholangiopancreatography (MRCP), the role of ERCP in solely imaging the pancreas will be relegated.

Pain, stones and strictures

In chronic calcific (tropical) pancreatitis, pain presents early and is the major clinical symptom. The etiology of pain remains debated: intraductal hypertension², increased pancreatic tissue pressure³, pancreatic ischemia⁴, neural inflammation⁵ and ongoing recurrent pancreatic injury have been described. Relief of intraductal hypertension and ductal drainage is the rationale for endotherapy in chronic pancreatitis. Associated increased pancreatic tissue pressure and repeated ischemia may interact further worsening the disease. Ductal

decompression may thus potentially delay progression of this disease. Additional causes of pain (pseudocyst and peptic ulcer disease) have to be excluded. Pancreatic cancer may complicate later stages of the disease⁶.

Patient selection for endotherapy is essential. Only a subgroup of patients with pain will benefit from endotherapy. A mandatory prerequisite is demonstration of a dilated pancreatic duct due to obstruction by a stricture or a stone, or both⁷. Drainage procedures are indicated only for patients with pain and marked morphological changes of chronic pancreatitis. An endoscopic classification for tropical pancreatitis has been proposed to aid in therapeutic decisions:

Table 1: Endoscopic classification of Tropical pancreatitis

Type I	MPD normal, only side branches involved
Type II	MPD dilated, no ductal strictures nor stones
Type III	MPD dilated, dominant stone or stricture in the head
Type IV	MPD dilated, stones throughout the duct without strictures
Type V	MPD grossly dilated, stones and strictures throughout the duct

Based on this classification, only patients with Type II – IV will benefit from endotherapy. Endotherapy will not benefit patients with only side branch involvement (Type I); patients with Type V will require surgical management.

Endotherapy for pain, stones and strictures revolves around the combined use of endoscopic pancreatic sphincterotomy (EPS), extracorporeal shock wave lithotripsy (ESWL), endoscopic stone extraction, and endoscopic stenting.

a) Endoscopic pancreatic sphincterotomy (EPS)

Endoscopic pancreatic sphincterotomy is used mainly to facilitate stone extraction. However, when only ductal dilatation is demonstrated (Type II), ductal decompression is achieved via EPS with or without stent placement. Endoscopic sphincterotomy of the pancreatic duct in patients

with chronic pancreatitis is a fairly safe procedure with a high technical success rate ⁸ .

The technique of EPS remains variable. At the Asian Institute of Gastroenterology (AIG), EPS is performed over a guide wire placed into the pancreatic duct. Pure cutting current is preferred to avoid further papillary fibrosis. The direction of the cut is between 12 to 2 o'clock (as opposed to the 11 o'clock direction of the biliary cut).

Other techniques have been described. Deviere⁹ describes a 2 step process: first biliary sphincterotomy and then pancreatic septotomy (dual sphincterotomy). Endoscopic biliary sphincterotomy (EBS) as the first approach has the advantage avoiding the rare biliary complication occurring after primary EPS: some patients present with jaundice the day after EPS probably due to edema occurring at the level of the biliary sphincter. After biliary sphincterotomy, the pancreatic orifice is usually seen at 5 o'clock on the margins of sphincterotomy. Its orifice can often be better visualized by sucking a little bit of air into the duodenum, inducing its transient opening. When deep cannulation of the MPD has been achieved, pancreatic sphincterotomy or "septotomy" is performed using pure cutting current. The cut is done with the distal part of the cutting wire, at 12 o'clock, over a length of 5 to 8 mm (depending on the diameter of the MPD) to create the largest access. The technique of a needle knife over an initially placed pancreatic stent is technically demanding in the setting of chronic calcific pancreatitis.

b) Extracorporeal shock wave lithotripsy (ESWL)

In the presence of pancreatic ductal stones (Type III and IV), ESWL is required in addition to decompression procedures. Without ESWL, deep cannulation of the main pancreatic duct fails in 50% of patients with severe chronic calcific pancreatitis ⁹ . Impacted pancreatic calculi are especially difficult to manage. While impaction at the ampulla can be promptly relieved by needle knife dis-impaction, those impacted within the duct are better managed by subjecting them to ESWL initially. Combined with minimally invasive endoscopic decompression, ESWL has replaced open surgery as the initial modality of therapy. Fragmentation rates with ESWL range from 75% to 100% and lead to

complete stone clearance in 40% to 75% of patients¹⁰⁻¹⁵. Factors favouring for treatment success include (i) single stones (ii) the absence of strictures and (iii) a small stone burden. Although complete pancreatic stone clearance is ideal, it is successful endoscopic decompression with reduction in main ductal diameters that is statistically correlated with pain relief^{16,17}. Following treatment, complete pain relief and a decrease in pain intensity is reported in 32-75% and 65-100% of patients respectively. ESWL fragmentation of pancreatic ductal calculi in conjunction with endoscopic clearance of the main pancreatic duct is associated with significant improvement in clinical outcomes in most patients with chronic pancreatitis.

In AIG, ESWL is performed with an electromagnetic lithotripter (Dornier Delta compact) equipped with a bidimensional fluoroscopic and in-line ultrasound "targeting facilities". Targeting of pancreatic duct calculi is performed via fluoroscopic guidance for radio-opaque stones. When radiolucent stones are found, targeting is performed via the ultrasound scanner of the lithotripter or fluoroscopically using a nasopancreatic tube. Shockwave energy settings are adapted to the individual patient's tolerance and comfort. The aim of therapy was successful fragmentation of ductal stones (to less than 3 mm) to allow spontaneous or endoscopic ductal clearance.

The use of epidural anesthesia has provided better patient tolerance of the procedure despite a higher intensity setting. In addition, epidural anesthesia reduces patient physical movement especially that of the lower limbs that facilitates targeting and fragmentation of the stones. Optimal efficacy and rapid fragmentation of stones is thus achieved.

Although multiple stones can be tackled by repeated sessions of ESWL in combination with endoscopic extraction, due to the high cost of therapy and uncertain outcome, we prefer to manage these patients surgically. In chronic calcific (tropical) pancreatitis, the stone volume is generally larger and the calculi are harder than alcohol related chronic pancreatitis.

ESWL may occasionally be deferred for patients with radiolucent stones. These "protein plugs" are usually friable and can be spontaneously

passed if their size is small following endoscopic sphincterotomy alone.

c) Endoscopic extraction of pancreatic calculi and pancreatic duct stenting

All patients undergo ERCP following ESWL. Complete ductal clearance is occasionally observed following ESWL alone. When residual stone fragments are present, EPS is performed and fragments are extracted using balloon catheters or dormia basket. Stone extraction is related to its size and the presence of downstream strictures. Pancreatic stent placement is required if dominant strictures are present or when main pancreatic duct clearance is deemed inadequate. In the presence of pancreatic duct strictures, endoscopic dilatation of the stricture combined with stent placement would benefit this subgroup of patients, at least in the short-term¹⁷. Patients who have difficulty with access to medical care or follow up have pancreatic stenting performed prophylactically. These stents are removed at 3-6 months post procedure.

d) Long term results of endotherapy

Pancreatic endotherapy is effective as short-term intervention, but the long-term result remains disappointing. The failure to ductal decompression to relieve pain in short term is consistent with the multifactorial etiology of pain in chronic pancreatitis. Surgical decompression provides immediate pain relief in 70-90% of patients. However, this diminishes with time so that only 50% of patients remain pain free at 5 years²⁰⁻²². In a long-term multicentre follow up study, ductal decompression offered relief of pain in two-thirds of patients when used as the only form of treatment. One-quarter of patients had to undergo surgery⁷. No long term-randomized trials are available comparing endotherapy against surgery.

Only a minority of patients remains symptom free after prolonged stenting. Therefore, careful follow-up is required. These stents require exchange for a period of 1 year either at 2-4 month intervals or "on demand" when pain recurs. A reduction or relief of symptoms may predict potential benefit from surgery.

Pseudocyst, pancreatic ascites and pancreatic pleural effusions

Endotherapy can be considered as first line treatment for pseudocyst adjacent to the upper gastrointestinal tract as it is safe, effective and provides promising long term results ²³ . Timing of endotherapy is best delayed approximately 4 weeks to allow the pseudocyst to mature. Earlier intervention may be necessitated by complications such as infection, hemorrhage, enteric or biliary obstruction, hydrothorax or uncontrolled pancreatic ascites.

Transmural drainage through the stomach (cystogastrostomy) is preferred for pseudocyst in the body and tail of the pancreas while those in the head are drained into the duodenum (cystoduodenostomy). An important concern in transmural drainage is potential bleeding from blood vessels interposed between the pseudocyst and gastroduodenal wall. Endoscopic ultrasound (EUS) or EUS-guided puncture of the pseudocyst eliminates this risk²⁴. When the cyst contains clear fluid, a 10Fr double pigtail stent will adequately drain the cyst. In the presence of necrotic debris, placement of a naso-cystic catheter for irrigation in addition to a 10Fr stent is required. When thick necrotic material is present, initial dilatation of the tract using a controlled radial expansion (CRE) balloon followed by removal of necrotic material with a dormia basket prevents subsequent clogging of the stent. EUS-guided cystenterostomy of nonbulging pancreatic fluid collections ²⁵ requires a cautious and skilled approach.

Transpapillary cyst drainage is preferred when cyst-duct communication is evident; complication rates are lower with transpapillary access (16%) than after the transmural approach (39%) ²⁶ . Stents may be placed into the pseudocyst ^{27, 28}; when technically not feasible, the stents should be advanced to the site of ductal communication as close as possible to the pseudocyst. In the presence of associated ductal disruptions, stents may either bridge the disruptions or be placed into the pseudocyst ²⁹.

Pancreatic ascites and pancreatic pleural effusions can be treated via placement of a transpapillary stent. In the presence of duct disruption or end fistula, the stent should be placed across the leak ^{29, 30} .

Biliary strictures complicating chronic pancreatitis

Bile duct strictures complicating chronic pancreatitis may be treated via endoscopic biliary stenting. Unfortunately, long-term results are poor and surgical bypass is preferred. When surgery is contraindicated, long-term placement of stents may be considered.

Pancreas divisum

It is estimated that 5-7% of the population has pancreas divisum. When found in association with chronic calcific (tropical) pancreatitis, a relative obstruction to pancreatic drainage through the minor papilla may contribute to the disease. In this setting, minor papilla sphincterotomy is potentially beneficial. Access for minor papilla sphincterotomy is more difficult and requires a "long position" of the duodenoscope. The use of special catheters (metal tip or tapered cannula) in addition to the use of hydrophilic (Terumo) guide wires is required.

Risk management

The need for patient selection and risk management requires reiteration. Contraindications to endotherapy include patients with duodenal stenosis and patients with multiple stones and strictures (Type V). When malignancy is suspected, further evaluation or surgery is warranted.

Pancreatic duct manipulations carry a more than 20% risk of inducing pancreatitis. Endoscopic pancreatic sphincterotomy carries a high risk of hemorrhage and perforation than its biliary counterpart³¹. It is thus cautioned that such interventions be performed only in large volume centers where expertise is available. Pancreatic duct stenting is associated with complications of stent migration, sepsis, perforation and ductal changes.

Minor reported complications of pancreatic ESWL are exacerbation of pancreatitis, mild abdominal discomfort and asymptomatic hyperamylasemia. Serious complications reported include hepatic subcapsular hematoma³², splenic rupture with life-threatening hemorrhage³³, splenic abscess formation³⁴ gastric submucosal hematoma, cholangitis, pancreatic related sepsis and fluid collections³⁵. Complication rates reported range from 0-20% of cases.

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