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Review Article

Management of chronic pancreatitis: Role of endoscopic therapy

Manu Tandan, D. Nageshwar Reddy

Department of Medical Gastroenterology, Asian Institute of Gastroenterology, Hyderabad, Andhra Pradesh, India

Abstract

Chronic pancreatitis (CP), a disease of varied etiology can, from the endoscopists perspective present as ductal strictures, stones, ductal leaks and fluid collections, biliary strictures or duodenal narrowing. This article deals with role of ERCP in the management of CP associated strictures and calculi. ERCP has a limited role in the diagnosis CP, though we feel that it is better at identifying small ductal calculi or leaks as compared to MRCP. Major and minor papilla sphincterotomy gives relief from pain in patients with mild or moderate ductal changes. Pancreatic ductal strictures are best managed by stenting. Use of multiple plastic stents (8.5-11Fr diameter) gives relief from pain in 84% and strictures resolution in 95% on follow up of over 3 years. CP associated CBD strictures are also managed by placement of multiple stents. Covered SEMS are increasingly being used in these strictures. Surgery is often the best option for CP associated CBD strictures which recur after adequate endotherapy. ESWL is the standard of therapy for pancreatic ductal calculi which are large, as seen in the tropics and the non alcoholic form of CP. Our experience has shown complete or partial clearance with ESWL in over 90% of patients with large PD calculi. Good pain relief was seen in both on short and long term follow up. In selected patients of CP, ERCP and endotherapy should be offered as first line of treatment, as the results are comparable to surgery. Prior endotherapy also does not interfere with subsequent surgical procedures.

Key words

Chronic pancreatitis, endoscopic pancreatic sphincterotomy, minor papilla sphincterotomy

Introduction

Chronic pancreatitis (CP) is a disease of varied etiology and is characterized by progressive and irreversible damage to the pancreas with resultant loss of both exocrine and endocrine functions. Irrespective of the etiology majority of patients of CP present with pain as the dominant symptom.

From an endoscopists perspective CP is a challenge. Patients of CP can present with ductal stricture, calculus, leaks, pseudocyst, duodenal narrowing, biliary strictures, GI bleed or a superadded malignancy.[1] Pancreatic endotherapy is performed in patient of CP who have failed or are unlikely to respond to medical therapy and is aimed at relieving pain or managing any of the above mentioned complications. The role of ERCP in CP associated strictures and calculi will be discussed in this chapter.

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Role of ERCP in Diagnosis of Chronic Pancreatitis

With the advent of endosonography (EUS) and magnetic resonance cholangio pancreaticography (MRCP) with or without secretin stimulation, the role of ERCP in the diagnosis of CP is minimal. ERCP has a sensitivity of 73-94% and specificity of 90– 100% in visualizing duct related changes.[2] In our experience ERCP is superior to MRCP in identifying ductal leaks and occasionally small ductal calculi. EUS is superior to

Address for correspondence:
Dr. Manu Tandan, Senior Consultant Gastroenterologist, Asian Institute of Gastroenterology, 6-3-661, Somajiguda, Hyderabad - 500 082, Andhra Pradesh, India.
E-mail: mantan_05@rediffmail.com

ERCP in early or less advanced CP with sensitivity of close to 100% as compared to 80% with ERCP.[3]

Role of ERCP in Treatment of Chronic pancreatitis and its Complications

Surgery has for long been the gold standard of treatment in patients of CP.[4] However with advances both in technique and technology, ERCP is being increasingly used as first line therapy in managing both pain and associated complications of CP. The advantages of endotherapy are as follows.[1,4-8] 1. Results comparable to surgery. 2. High success rate in properly selected patients. 3. Low morbidity. 4. Procedure can be repeated. 5. Age is a not a barrier. 6. Failed endotherapy is not a barrier to subsequent surgery.

In view of these advantages endotherapy should be offered as first line of therapy in selected patients of CP. A definitive response can be expected in 65% of patient with pancreatic ductal obstruction, 75% with pseudocyst and only 25% with CBD obstruction secondary to pancreatitis.[4]

Major Papilla Sphincterotomy

Endoscopic pancreatic sphincterotomy (EPS) is the only documented mode of therapy in patient with pain due to CP who have mild or moderate ductal changes according to the Cambridge classification.[9] This can be performed even in absence of ductal obstruction by stones or stricture. Over 80% of endoscopist performed the pull type of sphincterotomy. Rate of stenosis is around 15% and is believed to be less with the longer cut performed during the pull type procedure.[10] Even in patients with no stricture a 3 – 5 Fr single pig tail stent of 6 – 8 cm length is placed in the PD.[11] Spontaneous migration is seen in 80-90% of patients thus avoiding a second procedure. In the rest it is ideally extracted between 4 – 6 weeks.

A biliary sphincterotomy is performed in addition, under the following circumstances.[12]

a. Associated cholangitis
b. CBD>12 mm in diameter
c. Serum Alkaline phosphatase >2 times ULN.

Minor Papilla Sphincterotomy

Minor Papilla Sphincterotomy (MiES) was first performed by Peter Cotton over three decades ago. It is indicated in all patients where CP is associated with pancreas divisum or where there is an incomplete divisum with a dominant dorsal duct. Restenosis is seen in 20% of patients on a long term follow up.[13] Relief is seen in 41% of patient of pancreas divisum with changes of CP on imaging as compared to 33% in patients with chronic pain without CP and 77% of patient with acute recurrent pancreatitis.[14]

ERCP in Pancreatic Ductal Strictures

Pancreatic strictures are a common consequence of CP and could be due to inflammation or fibrosis. The resultant upstream hypertension is a common cause of pain. Successful relief of the obstruction by stenting results in relief of pain. Main pancreatic duct (MPD) strictures are defined high grade narrowing of MPD with at least one of the following.[15]

A. MPD dilated >6 mm beyond the stricture.
B. failure of contrast to flow through a 6 Fr naso pancreatic (NP) catheter
C. Presence of pain during continuous infusion of NP catheter with normal saline for 12 – 24 Hrs.

Dilatation followed by stent placement is the ideal therapy for isolated strictures in the head region. Multiple strictures with chain of lakes appearance as well as isolated strictures in tail are not amenable to endotherapy. Tight strictures are dilated with Teflon Bougie or a balloon catheter and a stent with a large diameter (7 – 10 Fr) is deployed.

Large stents have longer patency and are preferred over small caliber stents.[16] No agreement exists on stent diameter, type of stent, duration of stenting, frequency of change of stents in the absence of large experience.[1] The majority of patients who require restenting for pain recurrence after the removal of PD stents do so within one year and almost all of them in two years. Therefore if a patient remains symptoms free for 1 – 2 years after PD stent removal, he is likely to remain so for much longer periods.

Single large bore stents have been placed across the stricture and exchanged every 6 months or when the patients become symptomatic again. Relief is seen in 70 – 90% of patients on follow up of 14 – 69 months.[15] The study from Italy used multiple stents and followed the following protocol.[17]

1. Remove single stent
2. Dilate the stricture
3. Place maximum number of stents. Median of 3 stents of 8.5 – 11 Fr diameter used
4. Removes stents after 6 – 12 months.

Relief of pain was seen in 84% and stricture resolution in 95% on 38 months follow up.[17]

Pancreatic stents are associated with a variety of complications. Migration is seen in 10%.[18] Distal migration can perforate the opposite duodenal wall while internal migration is challenge for the endoscopist. Stent occlusion occurs over time.

Ductal changes have been reported with long term pancreatic stenting, though they may not have any clinical significance in patient of CP with pre existent fibrosis.[19] Newer 'wing' stent to prevent clogging or a 'S' shaped stent to prevent migration are under evaluation.[20,21]

Common Bile Duct Stricture

Common Bile Duct (CBD) strictures occur in 3–46% of patients with CP. and many of these patients remains asymptomatic.[22] Those strictures that are due to inflammation or pressure from a pseudocyst are reversible, while those due to fibrosis are not. Biliary drainage prevents development of secondary biliary cirrhosis and is indicated in presence of cholangitis or raised serum alkaline phosphatase persisting >4 weeks.

Results of Endotherapy have generally been unsatisfactory in CBD stricture due to fibrosis. Single stents produce relief in only 25% of patients.[23] Multiple plastic stents offered better resolution and relief in 90% of patients.[24] That dictum of 2 – 3 – 1 can be followed (2 stents placed simultaneously, changed every 3 months for 1 year). More than 2 stents can also placed and the same protocol followed. Surgery may be a better option for strictures which recur despite the above mentioned methods.

Self expanding metallic stent (SEMS) which are uncovered, partially covered or fully covered have been used in patients with resistant stricture and those unfit for surgery. They can also been used as a bridge to surgery as small length SEMS do not interfere with a subsequent surgical procedure.[25,26]

Pancreatic Calculi

Pancreatic ductal calculi are the end result of CP and occur in upto 50% of patients. Calculi in Idiopathic and Tropical pancreatitis are denser and larger as compared to those in alcoholic pancreatitis.[27,28] Small calculi <5 mm diameter in the MPD can be extracted by the standard technique of pancreatic sphincterotomy followed by basket or balloon trawl. Small baskets called spiral baskets are used for pancreatic stone extraction. Balloons are used infrequently as sharp stone edges and fragments tend to break the balloon. For calculi beyond a stricture, dilatation of the stricture with a bougie, balloon or Sohendra stent retriever prior to extraction becomes a necessity.

Larger PD calculi (>5 mm) are often impacted in the duct hence are not amenable to the standard technique for extraction. They need to be fragmented prior to expulsion or removal. Intra ductal mechanical lithotripsy requires encircling the stone and is not often feasible because of impaction. Success rate for mechanical lithotripsy in the pancreas are less than that for bile stones.[29] Intra ductal laser lithotripsy using a pancreatoscope or directly fluoroscopy is a difficult procedure and most reports remain anecdotal.[30] Balloon sphincteroplasty of the pancreatic sphincter to facilitate removal of large caculi has also been successfully reported in small series.[31] Extra corporeal shock wave lithotripsy (ESWL) has been extensively used for fragmentation for large pancreatic calculi and remains the procedure of choice.[26,27,32-36] Meta analysis has reported a success rate between 37 – 100% for ESWL for large PD calculi.[37] At our center, patients with large PD calculi in the head and body region with pain as their chief compliant are subjected to ESWL.[27] Patients with isolated calculi in the tail region, multiple MPD strictures, extensive calculi in head, body and tail, associated head mass, pseudocyst and pregnancy are excluded from ESWL. ESWL is performed successfully using a 3rd generation electromagnetic lithotripter with bi-dimensional fluoroscopy and ultrasonography targeting facility. Epidural anesthesia is used in the majority of patients. Of the 1006 patients who were subjected to ESWL followed by ERCP, a complete ductal clearance was achieved in 762 (76%) and partial clearance in 173 (17%) [Figures 1 and 2]. Significant relief in the pain score and decrease in analgesic requirement were seen in 84% of patients on short term follow-up. The side effects were minimal and mild; there was no procedure related mortality. Long term follow up to 8 years after the initial ESWL has shown a pain free response in 60% of patients and good relief in another 30% (Asian Institute of Gastroenterology, Unpublished data). Similar results with pain relief in 2/3rd of patients on long term follow up has been reported from other centers.[8,38] The protocol followed at our institute is given in Table 1. Radio opaque stones are subjected to ESWL directly under fluoroscopic control. For radiolucent calculi, which form a minority, a pancreatic duct sphincterotomy is performed and a naso-pancreatic tube (NPT) is placed. Contrast is passed through the NPT to help localize the calculi to fragments of 3 mm or less, so that they can be extracted at a subsequent ERCP. Stents are placed when the fragmentation

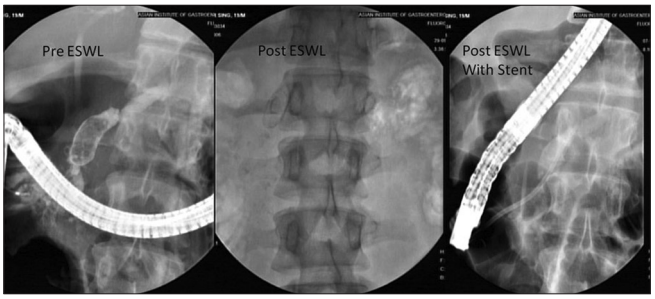


Figure 1: Large pancreatic calculi in head and genu, cleared by ESWL followed by pancreatic stenting[28]

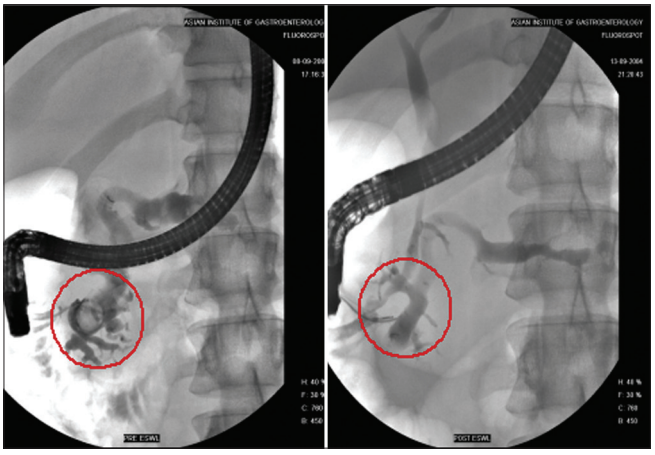
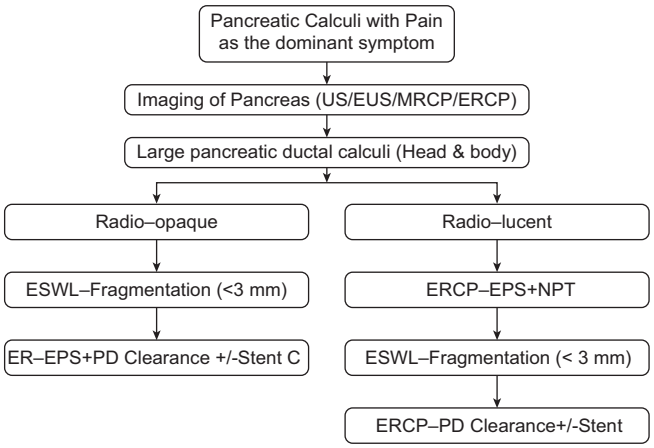


Figure 2: Single large PD calculus in head area. Post ESWL the calculus has cleared and PD has decreased in diameter[28]

Table 1: Protocol followed at Asian Institute of Gastroenterology, for ESWL of large PD calculi[7]



NPT: Naso Pancreatic Tube; EPS: Endoscopic Pancreatic Sphincterotomy; US: Ultrasound; EUS: Endoscopic Ultrasound; MRCP: Magnetic Resonance Cholangio Pancreatiography; ERCP: Endoscopic Retrograde Cholangio Pancreatiography

and clearance is incomplete or an associated stricture is present. A few studies have advocated use of ESWL alone followed by spontaneous expulsion of the fragments.[39,40] Amongst our patients with denser and larger calculi, we feel that endotherapy after adequate fragmentation of the calculi by ESWL helps in better clearance of the MPD. In conclusion, in a select group of patients of CP with large calculi, ESWL is a useful tool for fragmentation and this followed by endotherapy helps in PD clearance and relief of pain. Short term pain relief (less than 2 years) has been reported in 82-94% of patients, medium term pain relief (2 – 5 yrs) in 48-84% and long term relief in 60% of patients. A short duration of disease is associated with better relief.[37,38] Good clinical improvement has been associated with short duration of the disease and cessation of smoking.[37,38] It is therefore suggested that ESWL and endotherapy should be initiated as early as possible in the course of the disease. This will increase the possibility of better long term relief. Recurrence of pain is due to recurrence of stone formation, ongoing pancreatitis or any other mechanism of pain. Stone recurrence rate between 22% - 35% has been reported.[39,40] In the patients who have recurrence of stone formation or development of subsequent stricture retreatment is suggested. Endoscopic retreatment is usually easier as compared to the initial therapy and is equally effective.[7] This is in direct contrast to surgical approach which is associated with increase technical difficulty and morbidity when repeated.

The role of ESWL in exocrine and endocrine dysfunction is debatable. Conflicting reports on role of ESWL on patients with steatorrhoea exist. In our experience ESWL early in the course of disease benefits patients with clinical steatorrhoea. Further studies are needed to clarify the benefits of ESWL in diabetes. It is possible that early intervention in patients of pancreatic calculi can modify the course of the disease and avoid or defer the need for surgery as wells as prevent or minimize endocrine and exocrine dysfunction. Evidence from centers where ESWL is performed regularly show that relief from pain is seen in over 60% of patients on long term follow up.[8,38]

The role of ERCP in certain CP associated problems has been discussed in this article. However management of CP is a multidisciplinary task and needs active interaction between physician, endoscopist, surgeons and interventional radiologist. They play a complimentary role to each other and often more than one specialty is involved in the management of this patients. As mentioned earlier endotherapy is less invasive, can give good results can be repeated and doesn't preclude subsequent surgical procedures. It is advisable to offer endotherapy as the first line of management in selected patients with CP.

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