THE ROLE
OF
ENDOSCOPIC RETROGRADE CHOLANGIO PANCREATOGRAPHY
IN
TROPICAL CALCIFIC PANCREATITIS

DISSERTATION SUBMITTED FOR
DM
MEDICAL GASTROENTEROLOGY
(BRANCH- IV)
FEBRUARY-2006.

THE TAMIL NADU
DR. MGR MEDICAL UNIVERSITY,
CHENNAI, TAMIL NADU.

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CERTIFICATE

This is to certify that this dissertation entitled "THE ROLE OF ENDOSCOPIC RETROGRADE CHOLANGIO PANCREATOGRAPHY IN TROPICAL CALCIFIC PANCREATITIS" submitted by Dr. Thamarai Selvan Sivagnanam, to the Faculty of Medical Gastroenterology, the Tamil Nadu Dr. MGR Medical University, Guindy, Chennai-600 032, in partial fulfillment of the requirement for the award of DM., Degree Branch IV (Gastroenterology) is a bonafide work carried out by him under my direct supervision and guidance.

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INTRODUCTION

Tropical Calcific Pancreatitis (TCP) is the most common type in India and China, accounting for 60 – 70% of all Chronic Pancreatitis. This is in contrast with developed countries where Alcohol related Pancreatitis accounts for most of the cases of Chronic Pancreatitis. Tropical Calcific Pancreatitis is generally a disease of youth and early adulthood. It is found in areas with in 30 degrees of latitude on both sides of the equator. Pancreatitis is the most common mode of presentation in 70 – 100% of patients. Later in the course, patients may present with diabetes mellitus, maldigestion and weight loss. Pathologically Tropical Calcific Pancreatitis is characterized by large intra ductal calculi, marked dilatation of main duct and glandular atrophy. Its etiology is not known. High level of consumption of cassava which contains toxic glycosides is attractive hypothesis but not proved yet. Two recent studies have reported that a significant percentage of patients with Tropical Calcific Pancreatitis have spink1 mutation . Endoscopic Retrograde Cholangio Pancreatography (ERCP), the secretin stimulation test and Endoscopic Ultrasound (EUS) have all been suggested as a gold standard for the diagnosis of Chronic Pancreatitis. The management of Tropical Calcific Pancreatitis involves managing pain, diabetes and steatorrhoea.

Endotherapy has emerged as the main stay of treatment for pain. Surgery is an effective treatment for patients who had failed medical and Endoscopic

therapy. Drainage with lateral Pancreaticojejunostony is the most widely used procedure for ductal decompression.

This study is from an territory referral centre for gastroenterological, Hepatobiliary and pancreatic problems offering services free of cost to poor sections of the society. Endoscopic Retrograde Cholangio Pancreatography and Endotherapy was done by a team of experienced Endoscopists and assisted by residents. The records were well maintained. This forms the basis for this study.

LITERATURE REVIEW

TROPICAL CALCIFIC PANCREATITIS

INTRODUCTION:

The term “tropical pancreatitis” (TP) was coined in 1955 when Zuidema described 18 cases of disseminated pancreatic calcification in young nonalcoholic individuals in Indonesia. These patients were diabetic and had marked emaciation resembling kwashiorkor. Zuidema

considered this entity to be a degenerative disease of the pancreatic parenchyma (pancreatic cirrhosis) secondary to protein – calorie malnutrition[4].

Zuidema's patients were very poor and consumed a diet deficient in calories and protein. Non – ketotic diabetes mellitus of a severe degree was seen in almost all (16 of 18), and insulin resistance was common. Marked emaciation, parotid gland enlargement and hair and skin changes resembling kwashiorkor were some of the striking clinical features. A similar clinical picture, but without calcification of the pancreas, was noted in 27 other patients. It was assumed that these patients were suffering from fibrosis of the pancreas without pancreatic calculi. Nineteen of the 45 patients were less than 21 years of age. In spite of such advanced pancreatic disease, steatorrhoea was not seen.

Tropical calcific Pancreatitis (TCP) is seen in developing countries which affects young people, has a relatively accelerated course and is not associated with alcoholism. Various names have been proposed for this entity including tropical calcific pancreatitis, Afro Asian pancreatitis, tropical pancreatitis syndrome, nutritional pancreatitis and non-alcoholic pancreatitis. There were several reports of a similar syndrome from Asia (India, Ceylon, Thailand, Malaysia), Africa (Nigeria, Uganda, Burundi, Zaire and Malawi) and South America (Brazil). Shaper (1960) reported a similar syndrome in patients from Kampala, Uganda. The mean age of these patients with pancreatic calcification was 29 years. Neither alcoholism nor biliary tract disease were important clinical associations. The single largest series of cases of tropical pancreatitis reported to date is from the south western state of Kerala in India where Geevarghese and Pitchumoni observed this disease in endemic proportions in two major Medical College Hospitals of the state (Geevarghese et al 1962, Geevarghese and Pitchumoni 1966)[5,90]. Large numbers of patients were also reported from the state of Tamilnadu (Viswanathan 1980) from Orissa (Tripathi 1984, Tripathi and Samal 1987), and recently from Pune (Yajnik 1992). TCP is the commonest form of calcific pancreatitis in Southern India [96].

Fig.1.1 shows the distribution in TCP in India. Tropical calcific pancreatitis (TCP) in Southern India has the highest known frequency of the disease in the world[6]. Different aspects of TCP have been discussed in classic reviews (Geevarghese 1968, 1985, Narendranathan 1981, Pitchumoni 1984, Abu – Bakare et al 1986, Balakrishnan 1987, Mohan and Alberti 1990, Mohan et al 1990, Yajnik 1990, 1992)

DEFINITION:

TCP is a juvenile form of calcific, nonalcoholic pancreatitis found almost exclusively in developing countries of the tropical world. Idiopathic etiology was considered to be the most important diagnostic criterion of TCP. TCP is characterized by recurrent abdominal pain, exocrine pancreatic insufficiency, pancreatic calculi and diabetes. These patients are young, the calculi are larger and almost always intra ductal with an accelerated clinical course and there is no history of alcoholism.

PREVALANCE:

The prevalence of Tropical Chronic pancreatitis was 1:793 (0.12%) and that of Chronic calcific pancreatitis 1:1020 (0.09%) according to a systematic survey of 6079 families in a village in Quilon district in Kerala by Balaji in 1988. The prevalence of TCP was found to be very high in Southern India (80 to 140 per 100000 population) according to a study conducted by Department of Gastroentrology, AIIMS, New Delhi, India [19,96]. Our centre at Madras in Tamilnadu there are between 30 to 40 new cases of TCP each year. An other centre in Madras reported that TCP represents 1% of all diabetic patients that were registered[34].Distribution of tropical chronic Pancreatitis in India is shown in fig1.1.

AETIOPATHOGENESIS:

The following aetiological factors have been proposed for TCP:

Undernutrition

Cassava (tapioca) ingestion

Other dietary factors

Familial and genetic factors

Oxidant stress

Miscellaneous factors

Undernutrition:

Protein calorie malnutrition is present in many TCP patients and the role of undernutrition in the aetiology of TCP has been elegantly reviewed by Balakrishnan (1987) and Rao (1984)[8,94]. However, malnutrition could well be the effect rather than the cause, because calcific pancreatitis with consequent maldigestion and malabsorption could itself lead to protein calorie malnutrition. There are large pockets of malnutrition with relative infrequency of TCP, for example, Ethiopia (Lester 1984). This suggests that malnutrition by itself is unlikely to play an aetiological role. Thus the exact role of undernutrition in the aetiopathogenesis of TCP is far from clear.

Cassava:

The geographical distribution of TCP coincides with the areas of consumption of cassava (tapioca, manihot), a root consumed in tropical countries. Cassava is known to contain the cyanogenic glycosides

linimarrin and lotaustralin. Cyanide is normally detoxified in the body by conversion to thiocyanate. This detoxification requires sulphur which is derived from sulphur-containing amino acids. McMillan & Geevarghese (1980) showed that ingestion of cyanide led to transient hyperglycaemia in rats[5]. They concluded that their results supported a role for cyanide in the aetiopathogenesis of TCP. It must however be noted that none of the rats in the above experiments developed permanent diabetes. Moreover the effects were seen only with potassium cyanide and not with cassava. Thus the relevance of these experiments to the human situation is far from clear (Pitchumoni 1984).

Finally, Teuscher et al (1987) did not find any evidence of TCP in a rural West African population on a high cassava diet. While the cassava hypothesis might explain the occurrence in other areas where cassava is consumed, the possibility exists that other foodstuffs such as sorghum, ragi, jowar or certain varieties of peas may contain cyanide[28].

Other dietary factors:

Detailed studies on the dietary intake of TCP patients have been reported by Balakrishnan et at (1988). It was found that the protein intake in TCP patients was 53g/day, which was the same as controls. The fat intake of TCP patients and also of controls was very low in India (27g/day). It was concluded that a low fat intake could be one of the factors responsible for the occurrence of TCP.

Familial and genetic factors:

Pitchumoni & Geevarghese (1970) were the first to report on a large series of familial cases of TCP. They found 17 families where every other member had evidence of pancreatitis. The authors were unable to demonstrate any definite mode of inheritance in these families. Geevarghese (1985) has reported that about

8% of his TCP cases show evidence of familial aggregation. Familial aggreagation has also been reported by Balakrishnan (1984)[94].

Mohan et at (1989) have also reported familial aggregation in TCP. They found that, in some families, there was evidence of vertical transmission of the disease form the parents to the offspring; in other families there was a horizontal distribution among siblings. Familial occurrence suggests, but does not necessarily prove, a hereditary aetiology for TCP. Several family members could be exposed to the same environmental factors. However, a study from a group looking at gene makers has suggested for the first time a genetic basis for TCP (Kambo et al 1989)[97].

Micronutrient deficiency and oxidant stress:

Calcific pancreatitis in Caucasians has been linked to heightened oxidative detoxification reactions conducted by cytochrome P450-I within the pancreas and/or liver (Braganza 1988). Several factors may be involved, including calcific induction of the cytochrome P450-I subfamily of mono-oxygenases by xenobiotics (cigarettes, alcohol, occupational chemicals, dietary corn oil. Etc.,).

Further studies by Chaloner et al (1990) revealed that theophylline clearance (a measure of cytochrome P450-I activity in vivo) seems to be faster in TCP patients compared to controls. This suggested that oxidant stress may be playing a role in causation of TCP. Studies on antioxidant status of TCP patients showed low levels of vitamin C and beta-carotene (Mohan & Braganza 1991). This could also tilt the balance in favour of oxidant stress. These studies suggest that there could be common aetiological factors in temperate-zone and tropical forms of calcific Pancreatitis. A unifying hypothesis for alcoholic and tropical pancreatitis was proposed by Pitchumoni et at (1988). Perhaps in a background of genetic susceptibility to the disease, toxic factors in the diet may produce pancreatic injury leading to the endocrine and exocrine damage, thus accounting for diabetes and exocrine pancreatic dysfunction (Mohan et al 1991).

PATHOLOGY:

The pathology in pancreas in TCP has been described in detail by Geevarghese (1985) and Nagalotimath (1980)[5]. The pancreas is small, firm, fibrous and gritty to touch. Calculi of varying sizes and shapes may be detected in the ducts. The histopathology is quite characteristic with dilatation of the main ducts, pancreatic lithiasis, calcific inflammatory cell infiltration, fibrosis and atrophy of the parenchyma. Denudation of the ductal epithelium and squamous metaplasia may also be seen. Interlobular fibrosis is characteristically seen in early cases and focal, segmental or diffuse inter acinar fibrosis in more advanced cases. Islet cells are virtually absent but may occasionally be hypertrophied.

ANALYSIS OF STONES:

Stones consist of almost pure calcium carbonate. Pitchumoni et al (1987) have analysed the composition of pancreatic stones by X-ray diffractometry, scanning electron microscopy and energy-dispersive X-ray fluorescence[94]. They found that the nidus of the stone contains iron, chromium and nickel, whereas the outer shell contains calcium and 17 other elements. It is of interest that, irrespective of the aetiology of calcific pancreatitis, the structure and composition of pancreatic calculi are the same, suggesting a common path way for lithogenesis in TCP and Alcoholic chronic pancreatitis(ACP) patients revealed that the organic matrix contain one major pancreatic stone protein (PSP;Mol.Wt 15000) and a minor protein (Mol.Wt 30,000), the latter being an aggregate of the former. The presence of PSP in stones obtained from patients with TCP and ACP suggests that it may play a key role in stone formation during the course of

calcific pancreatitis of either aetiology[28]. PSP has now been renamed Lithostathine in view of its normal function of retarding calcium carbonate crystal growth.

CLINICAL FEATURES:

TCP is a disease of youth and the mean age at diagnosis of pancreatitis is 20 years. Over 90% of patients have onset below 40 years (Geevarghese 1968). Most hospital-based studies have reported a marked male predominance but Balaji (1988) found a slight female predominance in his population survey. Patients are invariably poor and present with extreme emaciation, protein calorie malnutrition, bilateral parotid enlargement and distension of the abdomen. Geevarghese (1968) has described a peculiar cyanotic colour of the lips but this is rarely seen in our patients. Growth is often retarded and multiple vitamin deficiencies and skin infections may be present. The natural history of the disease has been succinctly summarized by Geevarghese (1968) as abdominal pain in childhood, diabetes in youth and death at the prime of life[5]`.

Patients are often symptomatic for years before the diagnosis is established. The mean time from the onset of symptoms to diagnosis of TCP is 62 months.Though most individuals are lean, some are with a normal BMI or even obese. Typically, patients with TCP manifest with a triad of symptoms abdominal pain, maldigestion, and diabetes.

,

Abdominal pain

The frequency of abdominal pain varies from 30% to 95% in different series (Ramachandran et al 1969, BalaKrishnan 1984). The typical pancreatic pain is upper abdominal in location, may radiate to the back. It is initially severe, recurrent and episodic. The pain is usually aggravated by food. Abdominal ileus is a common accompaniment of this pain. In Geevarghese`s series 95% of patients had pain in the abdomen with radiological evidence of pancreatic calculi[5].

The precise mechanism underline the abdominal pain is uncertain. It may be related to an inflammation of the pancreas, increased intra pancreatic pressure due to an obstructed pancreatic duct secondary to stenosis or calcification, neuroinflammation or as a complication of the disease such as pseudocyst and obstruction of biliary or duodenal drainage. It tends to become milder and less frequent as the disease progresses over 10-25 years.

Exocrine insufficiency & Steatorrhea

The frequency of steatorrhoea is low because of the low fat intake in the diet.About 20% of patients complain of passing bulky, frothy or frank oily stools. If the fat intake is increased to about 100g day, over 70% of patients have demonstrable steatorrhoea(Pitchumoni 1984,Geevarghese 1985)[5,90]. Approximately 90% of the exocrine pancreas must be destroyed before significant steartorrhoea, azotorrhoea and creatorrhoea occur[20,21,23]. Fat maldigestion is more severe than protein and carbohydrate maldigestion. This is because lipid depends only on pancreatic lipase and co-lipase for digestion. Bicarbonate insufficiency causes reduced intraduodenal pH which is more injurious to lipase. Steatorrhoea is corrected even if 10% of the normal amount of lipase can be delivered at the proper time. Although maldigestion affects all nutrients, the most clinically significant problem concerns maldigestion of fat and fat-soluble vitamins.

Endocrine insufficiency

Diabetes mellitus develops when more than 80% of the gland has been destroyed. The diabetes is often complicated by hypoglycaemic episodes caused by an inadequate glucagon response during insulin therapy.
Diabetes is an invariable consequence of TCP. The World Health Organization study group report on diabetes mellitus (1985) has classified the form of diabetes secondary to TCP as a separate entity called

fibrocalculous pancreatic diabetes (FCPD) under the broad category of malnutrition related diabetes mellitus (MRDM).

Diabetes is usually severe with fasting blood glucose levels between 200 and 400 mg/dl. One of the characteristic features of this form of diabetes is that, despite requiring insulin for control of hyperglycaemia, patients rarely become ketotic. Mohan et al (1985) have shown that the response to therapy is dependant on pancreatic beta-cell function[98]. Patients who have some residual beta-cell function as shown by significant serum C-peptide levels may respond to oral hypoglycaemic agents and / or diet. At the other end of the spectrum are patients with absent or negligible C-peptide level and they may indeed be prone to ketosis. The majority of patients have enough beta-cell reserves to protect them against the ketosis but not sufficient to respond to oral agents.

Insulin resistance, defined as a daily insulin dose in excess of 200 units/ day is often described as a feature of this disease (Geevarghese 1968, WHO study group on diabetes mellitus 1985). The mean requirement of insulin dose was 40 $\pm$ 12 units per day. FCPD is a secondary form of diabetes and diabetic complications such as retinopathy, nephropathy and neuropathy occur during long-term follow-up (Mohan et al 1985) [11,98]. Macro vascular complications (Ischaemic heart disease and peripheral vascular disease), though rare, do occur (Mohan et al 1989). The relative infrequency of the Macro vascular complications are due to the younger age of the patients, leanness and the low serum cholesterol levels (Mohan et al 1985).

Malnutrition & Weight Loss:

This occurs initially due to a decreased caloric intake secondary to the fear and anticipation of abdominal pain (Postprandial exacerbation of pain) and later due to pancreatic exocrine insufficiency, maldigestion of fat, azotorrhoea, carbohydrate maldigestion, diabetes mellitus and malignancy.

Biliary Obstruction & Jaundice:

It is reported in 10% of TCP patients. Jaundice may occur due to biliary stricture secondary to inflammation of the pancreatic head or due to obstruction by a super imposed pseudocyst or malignancy[34].

Other common symptoms include nausea, vomiting, constipation, flatulence and bloating.

Rarely, patients may present with an abdominal mass, ascites or gastrointestinal bleeding[28,31,79].

Complications:

Multiple complications may be present in TCP. The presence of diabetes leads to increased frequency of pulmonary tuberculosis and fungal, skin and urinary tract infections (Pitchumoni 1984). Severe pyorrhea, gingivitis and bilateral cataracts are frequent associations. Hepatomegaly is common and cirrhosis of the liver may coexist. Obstructive jaundice is occasionally seen[35,36]. This is attributed to fibrosis involving the common bile duct or associated carcinoma of the pancreas[28].

Recently it has been observed that the frequency of carcinoma of the pancreas is very high in patients with TCP (Chari et al 1993). Initial studies suggest that the incidence of carcinoma in TCP may be higher than that noted in temperate zone pancreatitis[25].The incidence of pancreatic malignancy was reported as 8.6% (Philip Augustine 1986).

Addiction to Narcotics is a serious potential complication of TCP. Chronic pain with recurrent exacerbations is quite common. (Refer Table 1.6).

Investigations:

Serum amylase levels are usually within normal limits (Balakrishan 1984, Pitchumoni 1984). Occasionally the amylase levels may be elevated during an acute exacerbation of pain. In advanced stages of the disease the levels may be low. Serum lipase levels are generally low. Both serum cholesterol and triglyceride levels tend to be low (Mohan et al 1985)[98]. Serum total protein and albumin, serum calcium and phosphorus levels are all within normal limits. Serum Iron and D-Xylose absorption are normal.

Exocrine Pancreatic Function:

The paucity of data on exocrine pancreatic function in TCP is mainly due to unpleasantness and inconvenience of the older pancreatic function tests (Stool fat and tube tests). Recently, measurements of specific pancreatic enzymes (Serum and immunoreactive trypsin) showed the spectrum of exocrine pancreatic involvement (Yajnik et al 1989)[29]. In early cases Serum immunoreactive trypsin was sub normal in most cases and severely diminished in over two thirds. Stool chymotrypsin measurements showed similar results (Mohan et al 1989, Yajnik et al 1990).

The Secretin-Pancreozymin test in a small number of patients showed that pancreatic enzyme output was severely diminished; trypsin was more affected than amylase (Tripathy 1984, Tripathy & Samal 1987, Punnose et al 1987). Balakrishnan and colleagues (1988) made the interesting observations that even some of the control subjects from south India showed evidence of early Pancreatopathy. Yajnik also observed elevated Serum immunoreactive trypsin concentrations in our population in the absence of clinical or radiological evidence of TCP. It is possible that a subclinical pancreatopathy occurs in the tropics which

may have an environmental aetiology and that the full -blown picture of TCP with calculi is the extreme end of the spectrum (Yajnik et al 1990)[29].

Endocrine Investigations:

Several studies have attempted to explain the ketosis resistance exhibited by patients with FCPD. Mohan et al (1983) measured C-Peptide levels in these patients. It was found that patients with FCPD had partial preservation of pancreatic beta-cell function. In contrast, patients with classical ketosis-prone Insulin-Dependant diabetes mellitus had negligible beta-cell reserve. It was therefore concluded that the residual beta-cell reserve may be responsible for preventing ketogenesis in these patients. Recently Mohan et al (1990)reported that defective pancreatic glucagon secretion is responsible for ketosis resistance[98]. Glucagon one of the primary hormones responsible for ketogenesis, and an absent glucagon response could protect against ketoacidosis.

Yajnik et al (1990b) measured beta-cell function in TCP patients with different degrees of glucose tolerance. Plasma C-Peptide concentrations (A marker of pancreatic beta cell reserve) were normal in those with normal or mildly impaired glucose tolerance. In a diabetic group (FCPD) plasma C-Peptide concentrations were widely scattered; in about 75 % they were severely diminished, indistinguishable from type 1 diabetic patients. Interestingly, none of these FCPD patients had presented with ketosis, suggesting that other factors in addition to beta-cell function may be involved in the ketosis resistance shown by these patients[29].

Pancreatic Imaging:

1. Plain Roentgenogram:

Plain radiographs (fig.1.2) of the abdomen reveal diffuse or local pancreatic calcification in 72% to 97% of patients with TCP and in about 30% of patients with alcoholic

Pancreatitis[3]. TP is characterized by the frequent occurrence of large, discrete, dense calculi, patients with alcoholic pancreatitis has typically small, speckled calculi with irregular hazy margins. The stones may reach a large size of (4.5 cm) in diameter and have dumbbell- shaped extensions into the side branches that are difficult to remove at surgery[7,9,13]. Clearance of these staghorn-shaped calculi from the main pancreatic duct seems to be necessary to allow free drainage of the side branches into the main duct. Progressive displacement of calculi on serial plain radiographs may provide a clue to the presence of either an enlarging tumor or a pseudocyst in a patient with underlying CP[19].

2.Ultrasonography:

Ultrasonography helps to confirm the location of the calculi within the pancreatic duct. The pancreas is often reduced in size in patients with TCP. Additional features noted on ultrasonography are ductal dilatation, fibrosis of the gland and irregular gland margins (Mohan et al 1985b). The most common USG sign was a 'dilated pancreatic duct'[13]. Other findings included demonstration of calculi, increased echogenecity, pancreatic atrophy. USG findings in TP differ from the calcific alcoholic pancreatitis seen in the West; pancreatic calculi, pancreatic atrophy and duct dilation being commoner in TP (table 1.5)

The MPD is frequently visualized at ultrasound examination. However, body habitus and the presence of gas can occasionally frustrate sonographic interrogation. It is best seen in the mid body of the pancreas on transverse scans. Here the main duct is relatively anterior in location as it courses over the spine[15]. The duct is depicted by parallel ecogenic walls on either side of a relatively anechoic lumen. The normal side branches are usually not visualized, except for the occasional appearance of the larger uncinate branches in the pancreatic head. The MPD's diameter is less than that found at ERP. Ultrasound also probably under estimates the duct's diameter because of the apparent mural thickness imparted by the ecogenic duct wall. **Guidelines for average diameters of the head, body and tail have been reported as 3.0, 2.1, and 1.6 mm respectively**[17]**.**

3. Computed Tomography:

Computed tomography is also useful and the delineation of the pancreas is very good. However it is too expensive for routine use. The MPD is usually visualized on abdominal CT. The duct is displayed as a fine tubular structure of water attenuation, which can be followed over a variable distance against the background of the enhanced pancreatic parenchyma. As with the ultrasound, the normal side branches in the body and tail are not seen, but the occasional uncinate branch in the pancreatic head and the acessory duct may be visualized[13].

In TCP, the abdominal CT usually reveals irregularity of the contour on the gland, dilation of pancreatic duct and presence of calcification in patients with uncomplicated Pancreatitis[55]. CT is a useful adjuvant, particularly in detecting associated malignancy and to characterize the pseudocysts just prior to surgery. CT is superior to plain radiographs in detecting pancreatic calcification and to US in detecting pseudocysts with their anatomic relationships. CT and ultrasound are useful in instances where the MPD cannot be shown by ERCP due to the presence of large intraluminal calculi in pancreatic head causing an obstruction.

ENDO**SCOPIC RETROGRADECHOLANGIO PANCREATOGRAPHY(ERCP):**

ERCP remains the imaging method of choice in patients with suspected pancreatic disorders. ERP is mandatory in patients with TCP when surgical intervention is indicated. ERCP is indispensable in the differential diagnosis between inflammatory and new dysplastic changes within the pancreas.

Main Pancreatic Duct:

MPD has an S-shape contour with the straightened extension of the superior curve that course toward the left upper quadrant. The shoulder of the S-shape is called The “Neck”, the “Isthmus”, or the “Knee”. The

body of the pancreatic Duct extends from the Neck to the left border of the Vertebral Body, while the tail continues left ward to its termination. The MPD averages 16 to 17 cm in length (10-25 cm). The tail frequently ends in a terminal bifurcation to signal complete MPD opacification. The tail of the MPD is designated as proximal, or up-stream, while the head is distal, or downstream. The S-shape configuration, along with visualization of side branches, differentiates the MPD from the CBD(fig1.3). Occasionally, however, instead of an S-shape, the MPD contains a loop or spiral near the Duct Neck.

The diameters along the MPD vary because of its-tapered configuration. **The normal Pancreatic Duct diameters for the head, body and tail are 3.5, 2.5 and 1.5 mm, respectively**[46,54,57,58]**.** However the upper limits of the normal are more generous- 6.5, 5.0 and 3.00 mm, respectively. The normal Pancreatic Duct usually empties by 5 minutes after injection of contrast and over 10 minutes is considered abnormal.

Side Branches:

Quantifiable criteria for the pancreatic duct's side branches do not exist[18,93]. There is no standard number of standard pattern of branches arising from the MPD and number universally accepted side branch diameter or length. More important than a definable number of side branches is the periodicity of the branch points. This regular interval is usually constant in the body and tail of the MPD. The side branches should join at a reproducible interval. Whether the branch from the MPD at a right angle or at an acute angle, or join immediately opposite each other or alternate, the pattern is usually constant[52].

The side branch itself is a delicate, ductal structure that begets its own branches. It should gently taper as it courses into the parenchyma, being of widest dimension at its mouth. All the body and tail branches should appear uniform; however, the presence of two ectatic branches may still be considered normal. The side branches of the pancreatic head course inferiorly from the MPD to serve the uncinate process. This duct network consists of a dominant single branch with its own compliment of side branches or it may have a set of similar size the branches that fan out to cover this territory.

The second dominant side branch of the pancreatic head is the accessory duct, or the duct of Santorini. In 50 to 70% of cases, this duct maintains communication with the duodenum, draining through the minor papilla located 1 to 2 cm cephalad from the major papilla on the medial duodenal wall. In 1/3rd of cases, the accessory duct loses its connection with the duodenal, being relegated to serve as just another side branch off the MPD. Another variation in the side branch pattern is the occasional dominant branch off the body of the MPD that parallels parent duct as they course upstream[54]. In some cases it creates the appearance of a bifid or duplicated system.

ERCP in Tropical Calcific Pancreatitis:

ERCP is the best diagnostic method in patients with suspected TCP when the morphology of the pancreatic ductal system is of interest. This is particularly important when there is a possibility of co existent or associated biliary tract disease and when pancreatic surgery is contemplated[51]. The main diagnostic problems, as noted, arise in relation to recognition

of minimum degrees of TCP and in the differential diagnosis of chronic pancreatitis verses pancreatic carcinoma[25,38].

TCP causes a wide variety of morphological changes in the pancreatic ductal systems that are demonstrable by ERP(fig1.4). ERP provides important information concerning the functional status of the pancreas, the prognosis, the need for further therapy and the types of treatments that may be beneficial. There is a general correlation between the number and the types of ERP findings and the severity of TCP[11,18].

A system for staging ERP finding in Calcific Pancreatitis was proposed by Kasugai et al in 1972[53]. According to the system, three categories of chronic Pancreatitis were recognized by ERP. They are minimum, moderate and advanced (also referred to as grades I, II and III, respectively). In minimum CP, the radiographic findings are restricted to MPD branches and sub-branches and consist of irregular distribution, dilation, stenosis, and Obstruction. In moderate CP, the changes of mild degree are present but to a more advanced degree, and in addition, there may be cystic dilation of the MPD branches and also tortuosity, dilation, and stenosis of a mild degree of the MPD. In advanced Pancreatitis, all of the findings cited above are present in a more severe degree, and in addition, there may be obstruction or dilation of the MPD to cystic proportions (fig.1.5).

In 1984 the system for the Pancreatographic diagnosis of CP was set forth at the Cambridge International Workshop on Pancreatitis. Terminology and definitions for Pancreatographic abnormalities that arise in CP proposed at this conference have been summarized by Axon et al [1,52].

Assessment of MPD branches has pivotal importance in the Cambridge classification although this assessment is largely subjective. Abnormalities include a decrease in number (which may be focal, multifocal or diffuse), shortened, dilated, narrow and irregular contour. The term parenchymal opacification is preferable to acinarization, acinar opacification and acinar filling. This can be described as coarse, smooth or early. Axon et al recommended the terms Upstream (i.e., in the direction of the tail of the gland), in referring to proximal portions of a duct and downstream, to signify ductal segments nearest the duodenum. If the main duct diameter exceeds 1 cm, dilation is said to be severe. A localized narrowing less than 5 mm in length is referred to as a stricture. If there are multiple strictures, the duct is said to be severely irregular. Obstruction is premature termination of the MPD; this may be described as abrupt, tapered or irregular. Intraductal filling defects is a preferred term for stones and calculi. A non-ductal space that fills with a contrast is called a cavity. These may be large (> 10 mm in diameter) or small. Pancreatograms in CP are graded in the Cambridge system as normal or equivocal or as demonstrating mild, moderate, or marked changes, either diffuse or local (Table 1.1). The changes that were observed for assessing the severity or degree of CP based on Pancreatographic findings is presented (Table 1.2 and 1.3).

Heij et al compared ERP (Kasugai classification) and the results of Pancreatic function testing with secretin-cholecystokainin stimulation in 69 patients. In 86% of the patients, the results of the two tests were rated as comparable [2]. In some patients with CP, ERCP may fail to opacify the pancreatic duct. This can be due to faulty technique, stenosis or obstruction of the MPD near the main duodenal papilla. The

presence of long, distally tapering, smooth structure of distal CBD suggests the presence of advanced calcific pancreatitis.

The visualized filling defects within the pancreatic duct may be due to muco proteinceous substance or calcium carbonate stones. The muco gelatinous substance may be a prominent finding at the ERP and can cause ductal obstruction, which can be removed with manipulation[25,33].

ENDOSCOPIC ULTRASONOGRAPHY (EUS):

This is highly accurate in establishing the diagnosis of TCP and calcific Pancreatitis in general. EUS identifies both parenchyma and ductal changes. It has been used successfully in characterizing malignant pathology in TCP. EUS may be useful in following situations[87].

1. Equivocal CT findings for mass lesions (EUS-FNAC).
2. To delineate a local extension of malignant mass.
3. Technically unobtainable pancreatograms.
4. To identify the cyst and major vascular structures prior to Endoscopic drainage of pseudocysts.
5. Identification of small pseudocysts (less than 1 cm) or masses not identified by conventional imaging methods.

MAGNETIC RESONANCE CHOLANGIO PANCREATOGRAPHY (MRCP):

The main advantages of MRCP are non-invasive visualization of the biliary duct and pancreatic duct without injection of contrast, with no pre procedural preparation and no radiation to patients. It uses fast heavily T2-weighted pulse sequences to evaluate water containing structures such as gall bladder, bile ducts and pancreatic ducts. Thick slices can be obtained in a plane parallel to either the CBD or MPD so that the entire duct structure is depicted. Intra luminal filling defects, such as calculi are readily detected. MRCP is superior to CAT scan at depicting dilatation and beading of the MPD and may reveal calculi as intra luminal filling defects[22]. Like CAT scan, the sensitivity to side branch changes is much lower. Indications for MRCP included patients with surgical diversion of the stomach and duodenum, patients in whom it is not possible to opacify the duct proximal to an obstructing lesion and patients who are unlikely to require intervention during ERCP. Any cystic structure close to the pancreatico biliary tree will appear on MRCP whether or not it communicates[50].

MANAGEMENT:

Medical Management:

Medical control of pain

The main stay of treatment is analgesics. As the pain is continous and severe, there is a fine line between adequate analgesia and addiction[20]. Therapy may be initiated with acetaminophen or NSAIDS. Acetaminophen is given in the dose of 650 mg/po q 4 hr; dose and should not exceed 4000mg/d. Addition of Anti depressant such as amitriptyline hydrochloride in the dose of 25 to 75 mg PO qd may be helpful.

Pancreatic enzyme supplements are used for relief of abdominal pain and reducing symptoms related to steartorrhoea[44].

Hormonal therapy:- Octreotide is an 8 amino sequence containing the active portion of somatostatin. It is given as sub cutaneous injection in a dose of 50 to 200 micrograms tid before each meal. In a study by Toskes et al when compared with placebo the response to pain relief was 65% v 35%.

Celiac nerve block:- it can be done through percutaneous route under CT guidance and alcohol is injected to destroy the nerves around pancreas.

EUS guided Celiac plexus neurolysis:- It is first described in 1995. A linear phased array echo endoscope is passed into the stomach. The Celiac plexus is identified and a needle is positioned just lateral to the take off of the Celiac trunk, flushed, aspirated and injected with the local anaesthetic in combination with either steroid or absolute alcohol. In a study of 90 patients, Gress et al reported 55% improvement in pain score were seen.

Enzyme replacement therapy:- Pancreatic enzyme supplements are the main stay of therapy of TCP[44]. The goals of treatment with pancreatic enzymes in patients with TCP are two fold:

Pain relief

Control of maldigestion caused by exocrine pancreatic insufficiency

Pancreatic enzyme therapy is clinically given with the appearance of loss of body weight, steartorrhoea with stool fat excretion more than 15 gms per day, dyspeptic symptoms with strong meteorism, diarrhoea and in rare cases with the appearance of maldigestion of protein and carbohydrates and for the treatment of pain. Atleast 25000-30000 U of lipase per meal are necessary for adequate lipolysis to alleviate pancreatic steatorrhoea[20,44].

Dosage: 2-3 enteric-coated capsules or 4-8 non-enteric tablets after each meal. The capsules and minimicrospheres should be swallowed whole, without crushing or chewing. Treatment of pain is facilitated by the use of high protease enzyme containing preparation.

Future prospects: Recent scientific development such as the characterization of an acid stable bacterial lipase, the cloning of human acid stable lipase, the transfection of human lipase genes by virus mediator gene transfer and the development of very small acid stable lipase.

Adverse effects: Nausea, vomiting, bloating, cramping, constipation, diarrhoea, allergic reactions, hyperuricemia. In children with cystic fibrosis, fibrosing colopathy (strictures in right colon, fibrosis in terminal ileum) have been reported.

Control of Diabetes:-

The interval between onset of Pancreatitis and diabetes is reported to be an average of 9.1 years by a study from Kerala[89]. Diabetes in TCP presents most often in the third decade. The blood sugar level fluctuates very widely leading to episodes of hypoglycaenia. Nearly half the patients can be controlled on oral hypoglycaemic agents. Insulin resistance develops in 25% of the cases. Macro vascular complications are rare. Neuropathy seems to be a common feature. Most often TCP patients are non ketotic despite being insulin dependant[98].

Surgical Management:

The surgical management of TCP has been reviewed by Varghese (1980). Pancreatic drainage procedures have been found most useful in patients of tropical pancreatitis who have dilated ducts[63]. The drainage procedures include the following:

Pancreaticojejunostomy:

The Puestow-Gillesby procedure is the most frequently used drainage operation[61]. The choice is reasonable because, in order to clear the main duct of stones, the pancreatic duct has to be opened along its length[64]. Cysts located in the head or in the tail can also be brought into communication with the Pancreatojejunal anastomosis[61]. The Duval type of pancreatojejunostomy has been performed by some authors but others feel that this procedure is not suitable for cases of Tropical Pancreatitis[26].

Pancreatogastrostomy:

The results of this procedure are excellent; however, it is difficult to evaluate the advantage of Pancreatogastrostomy per se because it has been combined with postcoeliac neurectomy. The operation is easier to perform than pancreatojejunostomy and is also more easily undone if, at a later date, a reoperation becomes necessary. It also has the theoretical advantage of bathing the pancreatic duct in acidic secretion free from pancreatic enzyme activators. This could prevent a flare-up of pancreatitis in the immediate postoperative period[27].

Transduodenal sphincteroplasty:

The abnormalities of the pancreas in tropical pancreatitits affect the whole gland; surgeons were quick to realize that Transduodenal sphincteroplasty is grossly inadequate to drain the pancreatic duct[26,27].

Its use in patients with Tropical pancreatitis is confined to tackling lower-end common bile duct strictures, or combining with pancreatojejunal anastomosis when it was thought that the pancreatic duct in the region of the head of the pancreas could not be adequately drained retrogradely.

Pancreatic Resections:

Major resections have not been widely employed as a primary surgical procedure in Tropical pancreatitis[19]. The reluctance of most surgeons to perform major resections is based on the fact that the patients are usually young, not addicted to alcohol, and control of diabetes often requires massive doses of insulin.

Partial left-sided pancreatic resection involving removal of 25-50% of the pancreas has frequently been combined with a drainage procedure in patients with Tropical pancreatitis, the usual indications being presence of a mass or such severe distortion of the ductal anatomy in this area that adequate drainage was not technically possible.

Recurrence of pain after surgery. Recurrent pain after drainage procedures in patients with Tropical pancreatitis has often been reported. Stenosis of the anastomosis, retained calculi causing cysts or abscesses and internal post operative herniations sometimes twisting the Roux loop used for

the pancreatojejunal anastomosis are some of the causes identified for recurrence of pain[60]. Tumors are, however, the most important condition to be excluded in any patient with persistent or recurrent pain following a drainage procedure in Tropical pancreatitis[25,26].

ENDOSCOPIC THERAPY IN TROPICAL CALCIFIC PANCREATITIS

Therapeutic ERCP does not stand apart from diagnostic ERCP. One is an extension of the other. Endoscopic therapy is being applied in the setting of TCP patients presenting with pain,complications, and/or clinical episodes of acute Pancreatitis[30,31,32,78]. One of the aims of Endoscopic therapy is to alleviate the obstruction to exocrine juice flow. Endoscopic drainage is appealing in that it may offer and alternative to surgical drainage. Table 1.7 lists the available Endoscopic techniques and their complications.

Pancreatic ductal strictures:

Strictures of the main pancreatic duct may be a consequence of generalized or focal inflammation of necrosis around the main pancreatic duct. Outflow obstruction may be caused by ductal strictures, pancreatic stones, pseudocysts and papillary stenosis. Various Interventional Endoscopic procedures on the pancreatic duct have been attempted with variable success[99]. Dilatation of ductal strictures can be performed using dilators or balloons. Most often dilatation is followed by plastic stent placement across the stricture to ensure the patency. Dominant pancreatic strictures can be treated by Endoscopic stent therapy[72]. The success of this procedure has been reported to be 70% - 100%. Pain relief occurs in 55% - 100% of patients when followed for 2 – 69 months[12,51]. The best candidates for stenting are patients with distal stricture (in the pancreatic head) and upstream dilatation (type IV Pancreatitis). Most patients with the stricture have associated calcified pancreatic stones. For better results, the therapy must address both the stones and the stricture[60,63,70]

Pancreatic stents

They are standard polyethylene Amsterdam stents with extra side holes at 1 cm intervals to permit side branch juice flow. A pancreatic sphincterotomy is performed to facilitate placement of stents[65]. A guide wire must be maneuvered upstream to the narrowing. The diameter of the stent should not exceed the size of downstream duct. 5- to 7- French (Fr) stents are used in small ducts. 10- to 11- Fr stents can be used in patients with advanced calcific Pancreatitis and grossly dilated ducts[72,73,74].

Complications due to pancreatic stents are listed in Table 1.8.

Pancreatic ductal stones:

The rational for intervention is based on the premise that pancreatic stones increase he intra duct pressure and so the parenchymal pressure with the resultant pancreatic ischemia proximal to the obstructed focus. The pancreatic stone removal after sphincterotomy using conventional stone baskets, balloons and mechanical or laser lithotripsy with success rates ranging from 27- 100%[68,69]. Endoscopic shock wave lithotripsy (ESWL) is an adjunct to Endoscopic drainage[71,76]. Naso pancreatic tube may be used for flushing out stones as well as for irrigation with citrate for chemodissolution.

Endoscopic sphincterotomy

There are two methods to cut the pancreatic sphincter endoscopically[67].

1. A standard pull type sphincterotome (with or without guide wire) is inserted into the pancreatic duct and oriented along the axis of the pancreatic duct usually in 1 – 2 o' clock position. The cutting wire should not extend more than 6 – 7 mm inside the duct and the maximum cut should not exceed 5 – 10 mm.
2. Alternatively, a needle knife sphincterotome can be used to perform the sphincterotomy over a previously placed pancreatic stent.

Endoscopists are encouraged to remove pancreatic ductal stones in symptomatic patients or when the stones are located in the main duct head, body or both. The ability to remove a stone by Endoscopic methods alone is dependent on stone size, location, number, presence of downstream stricture, and the degree of impaction.

Factors favouring complete stone removal:

1. Three or less stones
2. Stones confined to the head or body of the pancreas
3. Absence of a downstream stricture
4. Absence of impacted stones

Largest stones (more than 1 cm), stones above the strictures and calcified stones can be fragmented within the pancreatic duct by extra corporeal shock-wave lithotripsy (ESWL)[71]. Protein plugs are soft and pliable and can be extracted immediately after the sphincterotomy. Largest stones can also be fragmented by intra ductal laser lithotripsy or with electro hydraulic lithotripsy with the help of a pancreatoscope.

Pancreatic Pseudocysts:

Pancreatic pseudocysts may complicate the course of TCP in 20 – 30 % of cases. The methods for Endoscopic drainage of pseudo pancreatic cysts include Endoscopic cystogastrostomy, cystoduodenostomy, and trans papillary drainage[32,80,81]. Endoscopic therapy is associated with a high technical success rate of 80% of patients and surgical drainage is required in approximately 10% of these patients.

Biliary Obstruction in Calcific Pancreatitis:

Biliary Obstruction can lead to cholangitis and eventually biliary cirrhosis. Intra pancreatic common bile duct strictures are reported to occur in 10% of patients with TCP[34,35]. Strictures are a result of fibrotic inflammatory restriction or compression by a pseudocyst. Plastic biliary stents are a useful alternative to surgery for short-term treatment of TCP induced CBD strictures and also high-risk surgical patients[82].

Future Role:

Endoscopic Management of TCP is technically feasible and should be considered as a valuable alternative to surgery in properly selected patients in proper hands. The future role of Endoscopic therapy will depend on evolving technology and the results of carefully performed randomized controlled trials that will address the clinical outcomes.

TABLE 1.1

CAMBRIDGE CLASSIFICATION OF PANCREATOGRAMS IN CHRONIC PANCREATITIS.

TERM	***MAIN DUCT***	***SIDE BRANCHES***	***ADDITIONAL***
		ABNORMAL	**FINDINGS**
Normal	Normal	None	-
Equivocal	Normal	Fewer than 3	-
Mild	Normal	3 or more	-
Moderate	Abnormal	3 or more	-
Marked	Abnormal	3 or more	One or more: large Cavity (>10 mm), obstruction, Filling defects, severe Dilation, irregularity

Modified from Axon AT, Classen M, Cotton PB, et al. Pancreatography in chronic pancreatitis: International definitions. Gut 1984; 25:1107-12.

TABLE 1.2

ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

FINDINGS IN CHRONIC PANCREATITIS.

DEFINITE FINDINGS

Irregular dilation of the main pancreatic duct, branches, and fine pancreatic ducts
Calculi
Cysts communicating with the main pancreatic duct with abnormal findings
Obstruction of the main pancreatic duct with abnormal findings

ABNORMAL FINDINGS

Irregular dilation of the main pancreatic duct, branches, and fine pancreatic ducts alone
Cysts communicating with branch ducts
Obstruction or stenosis, or both, of the branches and fine pancreatic ducts
Plugs (protein) within the ducts

REFERENCE FINDINGS

Simple dilation of the pancreatic ducts
Tortuosity of the main pancreatic duct
Localized stenosis of the main pancreatic duct
Rigidity of the pancreatic ducts
Coarse acinar opacification
Stenosis of the pancreatic portion of the common bile duct

Note: The pancreatic ducts include the main pancreatic duct, branches, and fine pancreatic ducts. Irregular dilation indicates dilation associated with stenosis (mainly relative degrees of stenosis).

TABLE 1.3

ASSESSMENT OF THE DEGREE (SEVERITY) OF CHRONIC PANCREATITIS BY ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY FINDINGS

	DEGREE OF FINDINGS		
FINDINGS	***Mild (MI)***	***Moderate (MO)***	***Severe (SE)***
Main pancreatic duct			
Irregular dilations	-	+ ~ + + +	
Calculi	-	-	+
Cysts	-	-	+
Obstructions	-	-	+
Plugs	+	+	+
Branches and fine pancreatic ducts			
Irregular dilations	+	+ +	+ + +
Calculi	-	-	+
Cysts	+	+ +	+ +
Obstructions	+	+ +	+ +
Plugs	+	+	+

Note: Bold face terms ***specify findings that are definite for chronic pancreatitis. These findings have priority importance in the interpretation of pancreatograms.***

**** including Cystic dilation.***

TABLE 1.4

COMPARISON OF RADIOLOGICAL FEATURES OF CALCULI IN TROPICAL PANCREATITIS AND IN ALCOHOLIC PANCREATITIS.

Radiological feature	***Tropical Pancreatitis (n = 89)***	***Alcoholic Pancreatitis (n = 32)***
Distribution (%)		
Right of vertebrae	***72***	***66***
Over vertebrae	***52***	***64***
Left of vertebrae	***70***	***82***
Right of vertebrae alone	***20***	***6***
Left of vertebrae alone	***2.2***	***20***
Size of largest calculus (%)		
< 10 mm	***65***	***18***
5-10 mm	***7***	***20***
< 5 mm	***28***	***62***
Margins of calculi (%)		
Sharp / well defined	***87***	***10***
Irregular / hazy	***13***	***90***
Radio density (%)		
+	***50***	***94***
+ +	***75***	***12***
+ + +	***62***	***12***

Reference: ***Chari S, Jayanthi V, Mohan V, Malathi S, Madanagopalan N, Viswanathan M. Radiological appearance of pancreatic calculi in tropical vs. alcoholic chronic Pancreatitis. J Gastroenterol Hepatol 1992; 7:42-44.***

TABLE 1.5

DIFFERENCES IN THE ULTRASONOGRAPHIC APPEARANCES OF TROPICAL AND OTHER TYPES OF PANCREATITIS.

Ultrasound Characteristics	***Tropical Pancreatitis***	***Other Pancreatitis***
Duct dilation	***82%***	***52%***
Presence of calculi	***77%***	***57%***
Pancreatic atrophy	***53%***	***5%***
Altered echogenicity	***59%***	***38%***

Reference: ***Bolordi L, Silvia LB, Gaiani S, et al. Sonography of chronic Pancreatitis. Radiol clin N Amer 1989; 27: 815-33.***

TABLE 1.6

COMPLICATIONS OF TCP.

STRUCTURAL	*METABOLIC*
Pseudocyst	***Narcotic addiction***
Pancreatic abscess	***Cobalamin (vitamin B12 Malabsorption)***
Pancreatic Ascites	***Sub cutaneous fat necrosis***
Common bile-duct obstruction	***Bone pain***
Duodenal obstruction	***Non diabetic retinopathy***
Splenic-vein thrombosis (Portal hypertension)	***Weight loss***
GI bleeding	***Diabetes related.***
Pancreatic cancer	***Poor quality of life.***

TABLE 1.7

ENDOSCOPIC INTERVENTIONS FOR TCP.

Clinical Condition	*Endoscopic Therapy*
Chronic Pancreatitis	***Endoscopic sphincterotomy (bile duct or Pancreatic duct)***
	Pancreatic stricture dilation
	Pancreatic stone extraction
	Pancreatic duct stone extraction after ESWL
	Bile duct stenting
	Pancreatic duct stenting
	EUS-guided celiac plexus block
Pancreatic pseudocyst	***Cysto enterostomy***
	Trans papillary pancreatic stenting
Pancreatic duct distruption / Ascites	***Trans papillary pancreatic stenting***

TABLE 1.8

COMPLICATIONS DIRECTLY RELATED TO PANCREATIC DUCT STENTS

Occlusion that may result in Pain, Pancreatitis, or both

Migration into or out of duct

Duodenal erosions

Pancreatic infection

Ductal perforation

Ductal; and parenchymal changes

Stone formation

AIM OF THE STUDY

TO STUDY THE ROLE OF

ENDOSCOPIC RETROGRADE

CHOLANGIO PANCREATOGRAPHY IN

TROPICAL CALCIFIC PANCREATITIS.

MATERIALS AND METHODS

A total of 123 consecutive patients (103M: 20F) in the age group of 13-54 years (mean age 29.8 years), diagnosed as Tropical Calcific Pancreatitis(TCP) in a tertiary referral centre for gastroenterological and hepatobiliopancreatic disorders. Patients referred and diagnosed as TCP by clinical, radiological, biochemical, Ultrasonographic, CAT Scan Evaluation (in selected cases) underwent diagnostic ERCP between Jan 2000 to Dec 2003 in purview of therapeutic ERCP.

ERCP was done using the ED 3430-T AO 1206 Video duodenoscope (Pentax) with a 2.8mm channel(fig2.1) and a conventional fiberoptic duodenoscope (Model FD-34B, A01085,FD-34V, A01086 and JF-1T10, JF-B4,110272) with 3.2mm channel. The Endoscopic suite is used in performing ERCP about ***900 sq.ft*** is adequate enough to handle all the radiological and Endoscopic equipment as well as the necessary personnel. A high quality television monitor of 525 lines is used for fluoroscopic visualization. Hard copy was obtained using spot films. A 9" * 9" cassette is the most frequently used size. The focal spot of the X-ray tube is 0.6mm. The X-ray tabletop moving in the horizontal plain to permit moving the sedated patient with minimal disturbance. Automatic tilting the X-ray table can help fill the intrahepatic bile-ducts at 15 degree head-down position. It can be tilted upto 90-degree upright position best for examining GB after it is filled with contrast medium. The radiographic examination of pancreatic duct and biliary tree begins with the plain 14" * 14" spot film to include the upper abdomen. The radiographic exposure for both fluoroscope and film images at 80 KVP and 90 KVP for the larger patient. The magnification factor for the machine is 36%. This is useful for measurement of stone size and length of a stricture.

Magnification factor = (Measured diameter of the duodenoscope) – (True diameter of the duodenoscope) / True diameter of the duodenoscope

Contrast:

60% concentration for opacification of the biliary tree and pancreatic duct. Full strength contrast 60% was used initially for diagnostic cannulation under fluoroscopic control until the tail and some side branches are visualized. Care was taken not to acinarize into the pancreatic parenchyma (pancreatic acinarization). The contrast used is meglumine salt of diatrizoic acid of 60% w/v with iodine content of 282mg/ml available as 20ml ampoules.

The pancreatic duct filled up to the tail and with a bifurcation as a landmark. Normally the biliary tree, excluding GB should be completely drained of contrast medium within 45 minutes and the pancreatic duct should empty within 5 to 10 minutes. When the filling of pancreatic duct is the primary concern but also if opacification of the bile-duct is required it can be filled atleast to the third-order intrahepatic bile-ducts.

Positioning of the patient:

It is performed with the patient lying most prone position with head turned towards right, shallow oblique position with the left side down or left lateral swimmer's position.

ERCP Procedure:

ERCP was performed as an inpatient procedure. Written and informed consent was obtained in all patients. The patient was on overnight fast and the procedure was preformed in the morning. A history of allergy to iodine contrast was noted. Intravenous sedation with 15 mg – 30 mg of Pentozocaine and / or 25 – 50 mg Promethazine was used. The patient was sedated with IV drugs via an IV Catheter inserted in the right forearm. A self-retaining mouth guard was placed and the patient was supported in a left lateral/semi prone position.

Hyoscine butyl bromide (Buscopan):

20 mg was given IV to relax the duodenum to inhibit duodenal peristalsis. Alternatively 0.5 mg glucagon may be used. Medication and contrast was drawn up in 20 ml disposable syringes and clearly labeled to avoid any mistake. 20 ml syringe with sterile water is useful for flushing the catheter prior to insertion of hydrophilic guide wire.

ERCP Instrument:

ERCP done using the ED 3430-T, A 1206 Video duodenoscope(Pentax)with monitor(fig:2.2 & 2.3). It is 12.5 mm in diameter with a 2.8 mm channel. Other conventional fibreoptic scopes,FD-34V(pentax) JF-B4,JF-1T 10(olympus) with 3.2mm channel were also used.

Personal protection:

Standard protection lead apron (0.2 mm to 0.5 mm lead) was used having front and back protection. A lead collar to protect the thyroid gland.

Accessories:

The cannula (6Fr Teflon tube which taper to a 5Fr tip). ERCP-1regular, ERCP-1-CT taper. Classic ERCP catheters are used for Endoscopic cannulation of the ductal system, injection of contrast and provides the ability to maintain wire guide access to the desired duct for the introduction of compatible devices. They are of 5.5 Fr in diameter require a minimum channel size of 2.8mm. A wire of 0.035" diameter can be passed through the catheter(fig 2.6).

Endoscopic sphincterotomy:

Routine blood counts and biochemistries are checked and coagulopathy corrected by vitamin K IM injection or transfusion of fresh frozen plasma. Patient should be advised to stop intake of asprin or NSAID and coumadin for one week prior to elective sphincterotomy.

Standard pull type sphincterotome CT-25m cotton cannulatome (WC 1 monofilamentwire, fig: 2.7). *The electrocautery wire, exposed only at the distal 1 to 2 cm of the catheter, is of differing lengths and constructed of either of a thin braided or monofilament solid wire, which can be seen at fluoroscopy. They accept 0.035" or smaller wire guides*

Needle knife sphincterotome -HPC-2 with 4 mm exposure wire .

The needle knife had reserved for high risk patients with a strong indication for accessing the ductal system when standard techniques failed. The needle extension on the HPC –3 may be adjusted by loosening the thumb screw or retracting the adjustable ring on the handle.

Guide wire (WC)

Teflon coated guide wire

THSF-35-400 .035" (regular and heavy duty),400cm,480cm.

Hydrophillic wire TM-400 - .035" tracer wire (coated with hydropolymer terumo that makes the guide wire very slippery when in contact with water).

Zebra wire .035" in diameter,260cm,450cm.(Zebra wire made of nitinol and is a multipurpose guide wire that can be used for accessing pancreatic duct,bile duct,for maintaining proper position during

sphincterotomy,for crossing the stricture,for mounting a 7-Fr stent directly over it and for exchanging over it various catheters and other accessories.It does not kink due its rigid nature.the tip is flexible and atraumatic.It has stripes for movement detection(fig: 2.8).

Glide wire .035", .021" in diameter,260cm,450cm.(Nitinol with polyurethane hydrophilic coat on entire length)

Stents

Pancreatic Stent Set (WC)

5Fr*7Fr 7,9,12 cm

Plastic stents are made up of Teflon Polyurethane or polyethylene. Pancreatic stents have many regularly spaced side holes(fig: 2.5).

Stent pusher

The choice of stent pushers depends upon the size of the stent to be placed .ie 7 Fr for a

7 Fr stent and 10 Fr for a 10 Fr stent.

Dilators

CDGC-8.5-7.5 Graded dilators

Push-type dilating catheters one inserted over a guide wire to dilate strictures. They have a metallic ring that indicates the position of maximum diameter nearest to the dilator tip. Biliary dilation catheters (Soehendra, Cotton, **Siegel-cohen** & Van andel). Available in a variety of sizes from 6Fr to 11.5Fr requiring a minimum channel size ranging from 2.8 to 4.2mm.

Balloon Dilators

Olbert biliary balloon dilators were used for dilating biliary strictures. They are available with various sizes and useful in dilating tight strictures(fig: 2.5).

Diathermy unit

Olympus PSD-10

Electrosurgical unit to the “off” position when it is not in use. Any electrosurgical accessory constitutes a potential electric hazard to the patient and the operator.

Adverse effects: Fulguration burns, nerve and/or muscle stimulation and cardiac arrhythmia. Utmost care was taken during operation.30W of cutting and10W of coagulation current was blended and used for electro surgical procedures and increased if needed.

Extraction basket

The extraction basket is used for the Endoscopic removal of stones. The basket is constructed of multifilament memory wire for shape retention. Contra indication includes an ampullary opening inadequate to allow the unimpeded passage of the stone and basket. The sheath of the WEB basket is 7Fr and requires a minimum channel size of 2.8mm.

RESULTS

Of 123 patients (103M: 20 F) with TCP were undergone a total number of 135 ERCP sessions. Diagnostic ERCP was performed in all 123 patients out of which 62/123 (50.4%) received pancreatic endotherapeutic interventions and 28/123 (22.7%) received biliary Endotherapy. The bile duct was cannulated in 88/123 (71.5%) patients and pancreatic duct in all patients (100%) and both ducts in 88/123 (71.5%) patients.

ERCP identified a wide variety of changes in the MPD and its side branches. It includes ductal irregularities 116/123 (94.3%), ductal dilatation 110/123 (89.4%), ductal strictures 85/123 (69.1%), ductal beading 56/123 (45.5%), cavities 18/123 (14.6%), Sacculation and Ectatic changes including chain of lakes appearance in 12/123 (9.7%) patients. Complications such as pseudocysts were noted in 11/123 (8.9%) and suspected pancreatic malignancy in 2/123 (1.6%).

A total of 62/123 (50.4%) patients had pancreatic Endotherapy of which 58/62 (93.5%) patients required Endoscopic pancreatic sphincterotomy. 37/62 (59.6%) patients received pancreatic stenting and 26/62 (45.1%) had undergone stricture dilatation.

Concomitant biliary changes in the form of biliary stricture was noted in 32/123 (26%) patients. Biliary Endotherapy such as biliary sphincterotomy in 21/32 (65.6%) patients, biliary dilatation 18/32 (56.2%) patients and biliary stenting were done in 16/32 (50%) patients.

16 patients received dual system Endotherapy of which 7/16 patients had stenting of both systems. Biliary stenting was done to facilitate pancreatic duct cannulation in 6 patients and removed after pancreatic Endotherapy.

Procedure related complications were noted in 6/123 (4.8%) patients and no mortality occurred. Refer Table 2.1.

TABLE 2.1

DIAGNOSTIC ERCP

Pancreatic	Biliary
Ductal calculi - 120/123, (97.5%)	Biliary stricture - 32/123, (26%)
Ductal irregularities - 110/123, (89.4%)	
Ductal strictures - 85/123, (69.1%)	
Ductal beaded appearance - 56/123, (45.5%)	
Cavities - 18/123, (14.6%)	
Sacculation and ectatic changes - 12/123, (9.7%)	
Pseudocysts – 11/123, (8.9%)	
Malignancy – 2/123, (1.6%)	

THERAPEUTIC ERCP

Pancreatic	Biliary
Endotherapy – 62/123, (50.4%)	Endotherapy – 28/123, (22.7%)
Pancreatic sphincterotomy – 58/62, (93.5%)	Biliary sphincterotomy – 21/32, (65.6%)
Pancreatic stenting – 37/62, (59.6%)	Biliary dilatation 18/32, (56.2%)
Stricture dilatation – 26/62, (41.9%)	Biliary stenting 16/32, (50%)

OTHERS

Dual system Endotherapy – 16 cases
Dual system stenting – 7 cases
Biliary stenting to facilitate PD cannulation – 6 cases
Complications – 6/123, (4.8%)

DISCUSSION

Tropical Calcific Pancreatitis is a special type of Chronic Pancreatitis prevalent in many parts of the Asia-Pacific region. The largest series is by Geevarghese from the State of Kerala, Southern India [5]. This present study is about 123 Tropical Calcific Pancreatitis patients (103M: 20 F) who were from different parts of the State of Tamil Nadu. Few patients (6/123) were from outside of this state. History significant Cassava Consumption not noted in our series since this is not the staple diet in Tamil Nadu. As noted in other series abdominal pain is the predominant symptom in the series (100%) of patients. The duration of pain ranges from 2 to 12.6 years with a mean duration of 3.8 years. No significant steatorrhoea noted in this series. Since the representing population of patients

from the lower social economic strata and it is related poor fat intake. Diabetes mellitus was noted in 3.2% of patients. 2.6% of patients received insulin for control. Lower incidence of Diabetes Mellitus in this series is in contrast to the studies from the same part of the State. It is primarily due to referral bias. Since this series is from gastroenterological special unit and other studies that reports the higher incidence of Diabetes Mellitus in TCP is from diabetes special clinic [98].

Most of the patients in this series have a lean body habitus with an average of BMI of 19.8. None of the patients in this series were obese as defined by BMI is > 30.

On screening pancreatic calcification is noted 120/123 (97.5%) patients. Compared with other series the percentage of patients with calcification in this series is high. This is again due to the referral bias and most of our patients have advanced diseased and mostly referred from other hospitals for tertiary care.

DIAGNOSTIC ERCP IN TCP:

Diagnostic ERCP in South India TCP patients have been documented since 1985 [6-10]. The diagnostic role and spectrum of ERCP changes in TCP can be considered as follows:-

a. To identify sacculation, ecstasia and beading
b. To identify ductal calculi in relation to its size, number, location, distribution, density variation and impaction
c. To identify pancreatic complications ascites or pleural effusion.
d. To differentiate and deliniate the plain X-ray findings of pancreatic calcification with the reference to the ductal or parenchymal location

e. To study biliary changes like stricture, compression and cholangitis related to TCP and its sequlae.
f. To identify the suspicious ductal malignant transformation
g. To formulate Endoscopic therapeutic interventions
h. To offer guidelines to consider surgical interventions
i. To evaluate symptomatic post operative cases
j. To plan Endosonographic evaluation
k. To collect pure pancreatic juice for research analysis
l. To plan manometric evaluation of the Sphincter of Oddi in selected situation.

In this series ERCP was done in 123 cases of Tropical Chronic Pancreatitis over a period of 3 years from 2000-2003 in the age group ranging from 13 - 54 years with a mean age of 29.8 years . The pancreatic duct was cannulated in all patients (100%) and the bile-duct cannulated in 88/123 (71.5%) and both in 88/123 (71.5%). The cannulation rate in Philip Augustine series [40] involving 130 patients was 87% for the pancreatic duct and 82% for the bile duct. The higher pancreatic cannulation rate was aided by the greater use of needle knife precut sphincterotomy. Failure to cannulate in TCP was due to: -

a. Impacted ductal stones
b. Tumour blocking the head portion of the duct
c. Distorted loco regional anatomy
d. Papillary stenosis
e. Compression by large pseudocysts
f. Large pancreatic calculi in the head region

The unrelated factors like periampillary diverticulae, ectopic ampulla, post gastric surgery states etc., add to the technical difficulties in cannulation. When ERCP fails ultra sound guided percutaneous pancreatic ductography (PPD) and percutaneous transhepatic cholangiography (PTC) can be considered in selected cases according to the clinical stage and situation. In this series cases with inability to cannulate pancreatic duct was not included.

Ductal changes:

ERCP identifies a wide variety of changes in the main pancreatic duct (MPD) and its side branches. It includes: - Ductal irregularities 116/123 (94.3%), ductal dilatation 110/123 (89.4%), ductal strictures 85/123 (69.1%), ductal beaded appearance in 56/123 (45.5%), cavities in 18/123 (14.6%), sacculation and ectatic changes in 12/123 (9.7%) were noted. Ductal strictures are localized having a short segment and may be single or multiple that occurs mostly in the head, genu and body portion. Long segment stricture (> 10 mm) is due to possible ductal malignant transformation. Strictures alternating beading to chain of lakes appearance, commonly seen in CP in the west is rare in TCP. It is noted in 5/123 (4%) patients. Filling defects are mostly due to ductal calculi 120/123. Ductal disruption and fistulae were seen in 3 cases. Ductal block had been documented in 108/123 (87.8%), predominantly due to intraductal calculi with or without strictures. The other causes of ductal block in TCP include malignant mass ± stricture, abscess/cyst and inflammatory mass. Ductal changes are focal when the involvement is less than one third and diffuse when the involvement is more than one third. In our series the ductal dilatations were graded as:-

a. Less than 10mm (11.6%)
b. 11-20mm (68.1%)
c. More than 20mm (20.3%)
a. Ductal dilatations up to and more than 50mm have been noted by Philip Augustine in Kerala suggesting that the largest pancreatic ducts are probably seen in TCP cases [11]. In 3.6% of our series grossly dilated ectatic changes involving the MPD and many side branches were noted in various sizes and forms resembling bronchiectasis and hence designated as **Pancrectasis** of TCP [30]. In cases where the entire ductal system has been opacified, the size and volume of the filled ductal system can be visually assessed.

Endoscopic methods and anastomotic surgeries are better suited for large ductal groups and resective surgery may be more ideal for the minimally dilated group. In addition serial analysis of ductal system changes will identify the ongoing changes and the complications, which alter the ductal morphology and continuity.

DUCTAL CALCULI:

Ductal calculi in TCP have a documented incidence of 72-100% [5,7].In our series it was present in 120/123(97.5%)of patients. The size of the calculi varies from 3-30mm. In this series the calculi were graded as: -

a. Less than 5mm (11.8%)
b. 6-10mm (36.4%)
c. 11-20mm (48.6%)
d. And more than 20mm (3.2%)

The calculi were sharp and well defined in (89.2%), irregular and hazy in (11.8%) and the distributions of calculi were Head region (69.8%), body (62.3%), tail (7.9%) and universal in (21.71%). Occasionally dumb-bell shaped extension of the calculi into the side branches have been noted. These stag-horn shaped calculi post technical difficulties in removal and mostly unsuccessful. Most of the calculi were very dense and can be differentiated from alcoholic calcific Pancreatitis [9]. Progressive displacement of calculi on serial studies may provide a clue to the presence of either an enlarging tumour or a pseudocyst. ERP has greater sensitivity in differentiating between the ductal and the parenchymal calcification identified in the plain X-ray. The calculi in TCP are always intraductal either in the MPD, side branches or both.

PANCREATIC COMPLICATIONS:

ERCP in TCP identifies some of the complications, which are also seen in the other forms of CP. Communicating pancreatic pseudocysts were seen in 6/123 (4.8%) and non communicating pseudocysts in 5/123 (4%) cases. Sarles has reported the preservation of pancreatic ductal epithelium for a longer time in TCP and hence the decreased incidence of cyst formation in these cases[56]. Pancreatic ductal disruptions in TCP are rare and when present ERCP has a definite role, which is of diagnostic as well as therapeutic significance. It was noted in 3 cases in this present series.

BILIARY CHANGES:

Biliary changes once considered very rare in tropical calcific Pancreatitis has now being increasingly documented[34,35]. Reported incidents ranges from 10-30%. In this series biliary changes are noted in 32/123 (26%) cases. TCP related benign biliary stricture in 30 cases and extraneous compression in 2 cases. In a study by Philip Augustine involving 150 cases of TCP, obstructive jaundice was detected in 16 cases[13]. Benign stricture of CBD in 4 cases (25%), pseudocysts in the head of the pancreas in 3 patients (18.7%) and cholangitis was present in 2 cases (12.5%). Large pancreatic calculi in the head region is another cause for biliary obstruction in 2 cases of TCP in this present series.

PANCREATIC MALIGNANCY:

TCP is considered as a premalignant condition[39]. The reported incidence ranges from 5-8.3%. It is predominantly a ductal adenocarcinoma and hence ERCP is useful. Augustine and Ramesh have put forth a series of TCP patients in which they have compared retrospectively various parameters between patients with tropical Pancreatitis (82 patients) and patients with super imposed malignancy concluded that mass lesion on ultrasound and ductal obstruction in ERCP were significantly associated with the presence of pancreatic cancer[13]. In our series suspicion of malignancy in 2 (1.6%) cases, the diagnostic ERCP findings were:- double duct sign in 1 patient, abrupt cut off of MPD in 1 patient and long segment stricture (> 10mm) in 1 patient .Shemesh et al have shown that pancreatic duct stricture of more than 10mm in length could diagnose pancreatic carcinoma in all 10 patients with coexisting Pancreatitis[38].

Diagnostic ERCP in TCP is useful in evaluating symptomatic patients following surgical procedures like pancreaticojejunostomy[26]. Collection of pure pancreatic juice after

stimulation with secretin and caerulin is possible[40]. ERCP with manometric evaluation is helpful in studying the sphincter pressure in TCP. Based on the diagnostic ERCP findings therapeutic options like non-surgical, endoscopic and surgical can be planned and implemented.

Based on the observations of diagnostic ERCP performed in view of possible therapeutic implications in this series have been grouped as follows:-

Group 1 – Ductal changes:

Irregularities stricture, dilatation, filling defects, blocks, sacculation, gross ductal dilatation involving the entire ductal system.

Group 2 – Calculi in MPD and side branches:

Size, location, margins, Density, distribution, type, Impaction and obstruction.

Group 3 – Complications:

Communicating pseudocysts, abscess, ductal disruption, pancreatic ascites and pancreatic effusion.

Group 4 – Malignant transformation:

Malignant stricture, mass, obstruction.

Group 5 – Biliary changes:

Biliary stricture, biliary compression, cholangitis.

Group 6 – Categorization of therapy:

Endoscopic, surgical, combined.

Group 7 – Considerations for other evaluations:

Endosonogram, manometry, pancreatic function studies and postoperative evaluation.

THERAPEUTIC ERCP IN TCP:

The diagnostic spectrum of ERCP in TCP provides a road map in selecting endotherapeutic interventions which is of clinical significance in relieving pain as well as exocrine insufficiency[23,30,40,41,43]. In India the endotherapeutic work of Nageshwara Reddy, Philip M, Krishna Rao, Deepak Bhasin, Nagarjuna, Subash, Maydeo, Nair and many others have established the utility and benefits of pancreatic Endotherapy in TCP. The main objectives of Endotherapy in TCP are :-

a. To relieve pain
b. To relieve pancreatic ductal obstruction
c. Removal of stones
d. To facilitate drainage of pancreatic juice flow

e. To improve pancreatic exocrine insufficiency

f. To treat complications

g. To avoid or postpone surgery.

ENDOTHERAPEUTIC PROCEDURES:

The different endotherapeutic procedures available for treating TCP patients in different clinical situations are classified into 3 groups:-

a. Pancreatic Endotherapy

b. Concomital biliary Endotherapy

c. Dual system Endotherapy.

ENDOTHERAPY FOR PAIN:

Sphincterotomy (pancreatic, biliary or both), pancreatic stenting and Endoscopic stone removal will significantly remove pain in TCP[25,60,62,67]. Biliary ductal hypertension secondary to TCP is another cause of pain even in the absence of jaundice and cholangitis. In that case, biliary Sphincterotomy and decompression can give significant relief of pain[65]. Biliary and Pancreatic Sphincterotomy $\pm$ pancreatic stenting were the common procedure done in this series (93.5%). Significant pain relief was achieved in (100%) of cases. Complications like pseudocysts, abscess, malignancy and pancreatic ascites contribute to pain, which may be relieved by pancreatic Endotherapy in selected cases[12,21,32,44,59].

ENDOTHERAPY FOR PANCREATIC STRICTURES:

The stricture in TCP can be dilated by Endoscopic methods using push dilators/balloon dilators in graded sizes after a preliminary sphincterotomy. In this series stricture dilatation was done in 26/62 (41.9%) cases. Even if Stricture dilatation is successful, placement of plastic stent following dilatation can give very good results[41,42]. It was done in all 26 (100%) cases. Failure to dilate the stricture in TCP is due to: -

a. Inability to cannulate the PD and place the guide wire (35.6%)
b. High grade and tight strictures (19.8%)
c. Strictures with impacted stones (28.7%)
d. Multiple strictures with a beading (12.1%)
e. Malignant long segment strictures (1.2%)
f. Inaccessible PD due to loco regional anatomical distortion (2.6%)

McCarthy et al have reported that pain relief that following dilatation and stenting in 70% of their patients[95].In our series patients with pancreatic strictures for whom pancreatic stenting was done were followed up for 6-36months and all of them had significant pain relief.

PANCREATIC STENTING (37):

Pancreatic stenting in TCP can be considered under the following circumstances:

a. With Sphincterotomy 35/37 (94.5%) patients
b. Without Sphincterotomy 2/37 (5.4%) patients
c. After stricture dilation 26/37 (70.2%)patients
d. After partially cleared pancreatic duct 10/37 (27%) patients
e. Stones in PD (100%)

f. In communicating pseudocysts 2/6 (33.3%)patients
g. In pancreatic disruption 2/3 (66.6%) patients
h. In pancreatic malignancy in TCP who are unfit for other procedures 1/37 (2.7%) patients

Amsterdam Plastic stents are usually deployed in sizes ranging from 7Fr – 10 Fr and length ranging from 5 – 12cm. Stenting is usually successful[71,72]. In our series distorted ductal anatomy prevented complete deployment in 6 (4.8%) of patients. Spontaneous migration was noted in 1 patient. Pancreatic stenting done in 37 cases in this series provide a significant pain relief in (96.4%) of cases. Mild post procedural abdominal discomfort was noted in (2.1%). Hence pancreatic stenting is an effective, relatively safe in experienced hands and also definitely indicated in symptom relief[30,42,43].The stent can be left in place until symptoms or complications. Alternatively it can be left in place for a period of 6 to 12 months with periodic exchanges[72,73]. Most of the patients in our series (98.2%) had no complications when followedup for more then 24 months.

CONCOMITANT BILIARY ENDOTHERAPY:

10-30% of TCP patients develop intra pancreatic CBD stricture mostly due to fibrosis in the head of the pancreas and rarely due to pseudocysts compression[34,90]. Not all radiological strictures need treatment. Biliary drainage is definitely indicated in patients having jaundice or cholangitis. In asymptomatic patients it is indicated if SAP is > 2 times normal for > 4 weeks in a patient with stricture. Biliary ductal hypertension in TCP presenting with pain responds to sphincterotomy and decompression. A study by Marc F, Catalano et al have concluded that multiple simultaneous stent pack technique appear to

be superior to single stent placement and may provide good long-term benefit and may obviate the need for surgical diversion procedures [86]. In our series biliary changes were observed in 32/123 (26%) of cases and concomitant biliary therapy was done in 28/32 (87.5%) cases with good relief. It included biliary sphincterotomy in 21/32(65.6%) cases, biliary stricture dilatation in 18/32(56.2%) cases, biliary stenting in 16/32(50%) cases. In 5/16 (31.2%) cases multiple stents were deployed and this CBD stent packing method gave very good relief and response in this series. Significant biliary decompression was achieved in 26/28 (92.8%) cases were documented by clinical and biochemical parameters. Metal stents were not used in this study due to benign nature of the disease and cost[84,85]. Endoscopic drainage has a good short-term outcome and also long-term outcome with sustained relief with routine plastic stents 10/16 (62.5%) cases in a mean follow-up of 2-4 years.

ENDOSCOPIC PANCREATIC STONE EXTRACTION:

Successful stone extraction can give a gratifying symptomatic relief of pain but technical difficulty and recurrence are problems to be addressed. A study by Rosch et al, a multicentric retrospective study of 758 patients of CP who received Endotherapy alone complete technical success could be achieved in 69%[76]. Outcome in stone and stricture groups was same. Small ductal calculi can be endoscopically removed. Endoscopic pancreatic sphincterotomy is considered as the corner stone [65,67]. Successful stone extraction after sphincterotomy depends on size, number, location and presence of associated strictures. Stones < 10mm located in head and body and 3 or less in number had a greater clearance rate. Ductal calculi upto 5-7mm can be removed with Dormia

baskets . Balloons are likely to be ruptured by the sharp fragmented spicules. Large impacted stones (1-1.5cm or more) need initial lithotripsy (electroshock wave, electro hydraulic, mechanical or laser) followed by Endoscopic methods by flushing or balloon retrieval. Lithotripsy techniques were not used in our series due to technical reasons. Removal of stones attempted in (29.1%) cases .In 28(23.3%)cases stones that less than 10mm were removed.

ENDOSCOPIC ENTERAL / TRANS PAPILLARY DRAINAGE:

Pancreatic pseudocysts complicate the course of TCP in ***20-30%*** of cases[81,82]. The indications for pseudocysts are the presence of symptoms, cyst enlargement, or complications. Large non-communicating bulging pseudocysts are indications for Endoscopic enteral drainage (Cystogastrostomy / cystoduodenostomy). However the incidence and literature documentation in TCP are anecdotal[90]. Trans papillary drainage can be done for large communicating pseudocysts. In this series Endotherapy in the form of trans papillary drainage was done for 2/6 (33.3%) cases of communicating pseudocysts. Internal pancreatic fistulas are an uncommon complication in TCP. These manifest either as pancreatic ascites or hydrothorax. Trans papillary pancreatic ductal stenting is an effective pancreatic Endotherapy[31,79,80,90]. In this series 2/3 (66.6%) cases had trans papillary pancreatic stenting for pancreatic ductal disruption.

DUAL SYSTEM ENDOTHERAPY:

Simultaneous and sequential Endotherapy of pancreatic and biliary system in TCP is necessary for technical and therapeutic issues especially in complicated cases with

malignancy and double duct sign[24] This was done in 16 cases in this series and dual system stenting in 7 cases.

Therapeutic ERCP in TCP:

ERCP has therapeutic potential and has got a dominating role in treating symptomatic TCP patients. Based on observations and experiences in our series, the role and the limitations of therapeutic ERCP in TCP patients can be approached and categorized into the following groups summarized below: -

Group 1: - Endotherapy for pancreatic duct related disorder like calculi, stricture and ductal hypertension.

Group 2: - Endotherapy for pancreatic complications like communicating pseudocysts and ductal disruption.

Group 3: - Endotherapy for concomitant biliary changes like biliary stricture, biliary compression, obstructive jaundice, and cholangitis.

Group 4: - Endotherapy for pancreatic ductal malignancy.

Group 5: - Endotherapy for symptomatic postoperative cases.

Group 6: - Endotherapy is not possible due to TCP related locoregional problems.

CONCLUSIONS

1. Tropical Calcific Pancreatitis is a very fertile area for applying different Endoscopic Retrograde Cholangio Pancreatographic interventions.
2. Diagnostic Endoscopic Retrograde Cholangio Pancreatography provides a road map for planning for different endotherapeutic procedures.
3. In Tropical Calcific Pancreatitis the calculi are always intra ductal and mostly multiple, dense and large and hence pose great technical difficulties for therapeutic Endoscopic Retrograde Cholangio Pancreatography.
4. Pancreatic stenting is an effective endotherapeutic procedure for the symptomatic relief of pain, improves ductal drainage and quality of life in Tropical Calcific Pancreatitis patients.
5. A new practically useful classification of diagnostic and therapeutic Endoscopic Retrograde Cholangio Pancreatography in Tropical Calcific Pancreatitis have been proposed for easy approach and planning therapy (subash classification).

6. Diagnostic Endoscopic Retrograde Cholangio Pancreatography before therapeutic Endoscopic Retrograde Cholangio Pancreatography provides a learning curve for future therapeutic endoscopists.

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APPENDIX

S.No		**Name**		**Gender**		**Age**		**Severity**	
							2000		
1		Mrs.Jamuna Rani		F		34		Grade IV	
2		Mr.Sathish		M		20		Grade IV	
3		Mrs.Banu		F		38		Grade IV	
4		Mr.Doss		M		38		Grade IV	
5		Mr.Varadhan		M		30		Grade III	
6		Ms.Jothi		F		13		Grade IV	

7		Mr.Periyasamy		M		38		Grade III	
8		Mr.Srinivasa Perumal		M		30		Grade IV	
9		Mr.Baskar		M		21		Grade III	
10		Mr.Dinakaran		M		30		Grade IV	
11		Mr.Ramalingam		M		40		Grade IV	
12		Mr.Tirumalai		M		12		Grade IV	
13		Mr.Rajendran		M		30		Grade IV	
14		Mr.Balamurugan		M		20		Grade IV	
15		Ms.Kalaivani		F		16		Grade III	
16		Mrs.Chinnamma		F		35		Grade IV	
17		Mr.Saravanan		M		26		Grade IV	
18		Ms.Vani		F		16		Grade IV	
19		Mr.Mohan		M		31		Grade IV	
20		Mr.Loganathan		M		38		Grade III	
21		Mr.Murugan		M		29		Grade III	
22		Mr.Padmanabha		M		27		Grade IV	
23		Mr.Rajesh		M		25		Grade IV	
24		Mr.Kamaraj		M		35		Grade IV	
25		Mr.Swaminathan		M		31		Grade IV	

26		Mr.Kuppusamy		M		40		Grade IV	
27		Mr.Ramasamy		M		37		Grade IV	
28		Mr.Purushottaman		M		24		Grade IV	
29		Mr.Swaminathan		M		31		Grade IV	
30		Ms.Rubavathy		F		14		Grade IV	
31		Mr.Mohan		M		36		Grade IV	
S.No		**Name**		**Gender**		**Age**		**Severity**	
32		Mr.Chandran		M		46		Grade IV	
33		Mr.Periyasamy		M		13		Grade IV	
34		Mr.Saravanan		M		30		Grade IV	
35		Mr.Chandrasekar		M		44		Grade IV	
36		Mr.Gnanaraj		M		48		Grade IV	
37		Mr.Govindaraj		M		49		Grade IV	
38		Mrs.Parvathy		F		35		Grade III	
39		Mr.Murugesan		M		35		Grade IV	
40		Mr.Senthil		M		13		Grade IV	
41		Mr.Mani		M		40		Grade IV	
42		Mr.Seethapathy		M		36		Grade IV	
							2001		

43		Mrs.Lakshmi		F		55		Grade IV	
44		Mr.Srinivasa Perumal		M		30		Grade IV	
45		Mr.Babu		M		39		Grade IV	
46		Mr.Doss		M		38		Grade IV	
47		Mr.Venkatesh Kumar		M		31		Grade IV	
48		Mr.Ekambaram		M		45		Grade IV	
49		Mr.Venkateshwar		M		31		Grade III	
50		Mr.Samrajiam		M		32		Grade IV	
51		Mr.Bakthavatchalam		M		37		Grade IV	
52		Mrs.Kasthuri		F		42		Grade IV	
53		Mr.Kirubakaran		M		41		Grade IV	
54		Mr.Srinivasan		M		30		Grade IV	
55		Mr.Damodaran		M		30		Grade IV	
56		Mr.Gunasekar		M		23		Grade IV	
57		Mr.Baburaj		M		32		Grade IV	
58		Mr.Kumar		M		21		Grade IV	
59		Mr.khader		M		32		GradeIV	
60		Mr.Murugesan		M		32		Grade IV	
61		Mr.Kaliappan		M		18		Grade	

								IV	
62		Mr.Srinivasan		M		40		Grade IV	
63		Mr.Munisamy		M		42		Grade IV	
64		Mrs.Irfana Begum		F		25		Grade IV	
S.No		**Name**		**Gender**		**Age**		**Severity**	
65		Mr.Baskar		M		30		Grade IV	
66		Mr.Edward		M		20		Grade IV	
67		Mr.Selvaraj		M		38		Grade IV	
68		Mr.Kesavan		M		25		Grade IV	
69		Mr.Mohan		M		38		Grade IV	
70		Mr.Karthik		M		24		Grade III	
71		Mr.Babu		M		34		Grade IV	
72		Mr.Sekar		M		37		Grade IV	
73		Mr.Baskar		M		16		Grade IV	
74		Mr.Sathiyaraj		M		17		Grade IV	
75		Ms.Vijaya		F		20		Grade IV	
76		Mr.Murugan		M		32		Grade IV	
77		Mr.Perumal		M		26		Grade IV	
							2002		

78		Mr.Baskar		M		16		GradeIV	
79		Mr.Parasuraman		M		37		GradeIV	
80		Mr.sankar		M		30		GradeIV	
81		Mr.kandasamy		M		32		GradeIV	
82		Mr.swaminathan		M		31		GradeIV	
83		Mr.kandasamy		M		20		GradeIV	
84		Mr.thirumurugan		M		16		GradeIV	
85		Mr.balachandran		M		27		GradeIV	
86		Mr.Kalaiarasi		F		29		GradeIV	
87		Mr.Mahendran		M		37		Grade IV	
88		Mr.Senthilvel		M		32		Grade IV	
89		Mr.Venkateshwaran		M		35		Grade IV	
90		Mrs.Vasantha		F		46		Grade IV	
91		Mr.Kathiresan		M		18		Grade IV	
92		Mr.Chandrasekar		M		30		Grade IV	
93		Mrs.Anusha		F		22		Grade IV	
94		Mr.Rajesh Kumar		M		15		Grade IV	
95		Mr.Mani		M		32		Grade IV	
96		Mrs.Sulochana		F		50		Grade IV	
97		Mr.Prasanth		M		19		Grade IV	

S.No		Name		Gender		Age		Severity	
98		Mr.Sathyaraj		M		17		Grade IV	
99		Mr.Bamanam		M		45		Grade IV	
100		Mr.Shanmugam		M		35		Grade IV	
101		Mrs.Loudumary		F		25		Grade IV	
102		Mr.Rajan		M		18		Grade IV	
							2003		
103		Mr.Kotteswaran		M		28		Grade IV	
104		Mr.Muthuraman		M		54		Grade IV	
105		Mr.Manikandan		M		10		Grade IV	
106		Mr.Kalanjium		M		42		Grade IV	
107		Mr.Raveendran		M		18		Grade IV	
108		Mr.Sivaperumal		M		30		Grade IV	
109		Ms.Veerammal		F		14		Grade IV	
110		Mr.Kasi		M		32		Grade IV	
111		Mr.Kuppuraj		M		14		Grade IV	
112		Mr.Devarajan		M		45		Grade IV	
113		Mr.Loganathan		M		31		Grade IV	
114		Mr.Saravanan		M		15		Grade	

								IV	
115		Mr.Ramanathan		M		14		Grade IV	
116		Mr.kandasamy		M		32		Grade IV	
117		Mr.Sekar		M		30		Grade IV	
118		Mrs.Jasmine		F		21		Grade IV	
119		Mr.thirumalai		M		36		Grade IV	
120		Mr.muthusamy		M		23		Grade IV	
121		Ms.muniamma		F		17		Grade IV	
122		Mr.Arun		M		31		Grade IV	
123		Mr.Doss		M		30		Grade IV	