Surgical Globetrotting

Prospective Study of Pancreatic β-cell and Exocrine Function following Duct Decompression in Tropical Calcific Pancreatitis

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Abstract. Tropical calcific pancreatitis (TCP) is a chronic, nonalcoholic pancreatitis, which is limited to developing countries. In this condition, surgical decompression of the pancreatic duct consistently leads to relief of abdominal pain. However, no data are available on the effect of such intervention on pancreatic function. The aim of the present study was to prospectively evaluate β-cell and exocrine function following ductal drainage in patients with TCP. We studied 14 consecutive TCP patients who underwent ductal decompression for abdominal pain (longitudinal pancreaticojejunostomy in 12 patients, endoscopic sphincterotomy and ductal stenting in 2 subjects). Six patients who refused similar intervention served as controls. Patients were evaluated prospectively (median follow-up 13 months) for pain score, fasting and oral glucose stimulated plasma C-peptide [mean ± SEM] 0.41 ± 0.08 vs. 0.42 ± 0.05 nmol/l; peak plasma C-peptide 2.24 ± 0.20 vs. 2.32 ± 0.24 nmol/l). Fecal chymotrypsin was diminished in all patients prior to intervention (1.9 ± 0.7 U/g), and did not normalize after ductal drainage in any subject. Serum trypsin levels were variable, being elevated in 29% and diminished in 47% of subjects. All 4 subjects with elevated baseline trypsin levels had a sharp fall after intervention (1020 vs. 175 ng/ml). However, serum trypsin did not normalize after ductal drainage in any patient with a diminished baseline value. In conclusion, patients with TCP have significant reduction in abdominal pain after decompression of the main pancreatic duct. However, there is no significant change in β-cell function. A fall in elevated serum trypsin suggests that there may be relief of subclinical inflammation after intervention; however, there is no improvement in exocrine function after a follow-up of 1 year.

Tropical calcific pancreatitis (TCP) is a unique form of chronic, nonalcoholic pancreatitis, which is limited to the tropical developing countries [1, 2]. Patients present at a young age with severe abdominal pain, weight loss, and insulin-requiring diabetes [1–6]. Suspected etiological factors include intake of cyanogenic glycosides (such as in cassava) and protein-calorie malnutrition [1, 2, 7].

The pancreas is often shrunken with dilatation of the main pancreatic duct due to multiple intraductal calculi and strictures [8, 9]. At the time of presentation, patients have markedly diminished pancreatic exocrine function and a variable β-cell reserve [1, 10, 11].

The exact pathogenesis of pain and progressive pancreatic dysfunction in chronic pancreatitis is not clear [12]. Increased intraductal pressure, and its effect on the pancreatic parenchyma, may play a role in a subset of patients who present with dilatation of the pancreatic duct due to stones or strictures [13]. In these patients with “obstructive pancreatitis,” the pain responds well to decompressive procedures, suggesting that the raised ductal pressure plays a pathogenic role [14, 15]. It has also been shown in some studies that early drainage may preserve pancreatic function better than conservative management [16, 17]. The most common decompressive procedure is the side-to-side longitudinal pancreaticojejunostomy (LPJ, modified Puestow procedure) [18, 19]. This operation is reported to control pain successfully in > 80% of patients with chronic alcoholic pancreatitis [14, 15]. An alternative drainage procedure in cases of proximal duct dilatation, endoscopic sphincterotomy and stenting of the pancreatic duct, also relieves pain successfully [20].

Although there are only a few reports of pancreatic duct decompression in subjects with TCP, the results of LPJ are encouraging, with pain relief in about 80%–90% of patients [20–23]. However, no data are available on the effect on pancreatic function. Therefore, we conducted a prospective study to evaluate the effect of drainage of the pancreatic duct on β-cell and exocrine function in TCP patients.

Materials and Methods

Selection Criteria

TCP was diagnosed on the basis of: (1) history of recurrent abdominal pain; (2) dilatation of the main pancreatic duct with intraductal calculi; (3) exclusion of alcohol intake (by history) and
other secondary causes of chronic pancreatitis such as obstructive biliary tract disease, hypertriglyceridemia, and hypercalcemia (by appropriate investigations).

Patients and Controls

All TCP patients with pain of moderate to severe intensity, seen in our hospital between January 1997 and July 1998, were offered a decompressive procedure. Fourteen patients gave consent for ductal drainage. TCP patients who refused any intervention, but were willing to come for follow-up evaluation (n = 6), were recruited as controls. All patients were North Indian, and most belonged to the state of Uttar Pradesh. All patients and controls gave informed consent, and the study was approved by the institutional ethics committee.

Decompressive Procedures

In 12 patients a modified Puestow (Partington–Rochelle) procedure was performed [19]. The dilated main pancreatic duct was opened along its entire length, stones were removed, and a longitudinal side-to-side Roux-en-Y pancreaticojejunostomy was performed. For patients with stones in the uncinate process, or with an enlarged/bulky pancreatic head, coring of the head (Frey’s procedure) was performed to ensure complete ductal clearance and adequate drainage [24]. Ancillary procedures were performed at the same time as indicated (Table 1). In 2 subjects, in whom a single stone was present in the proximal part of a uniformly dilated main pancreatic duct, endoscopic sphincterotomy and ductal stenting was performed.

Study Protocol

All patients underwent a detailed clinical evaluation. A scoring system was used to grade the pain, in which pain intensity, frequency, and its consequences were each scored from 1 to 8 [5]. All subjects underwent abdominal ultrasonography and contrast enhanced computerized tomography of the pancreas. Endoscopic retrograde cholangiopancreatography was performed in 6 patients.

Diabetes was diagnosed on the basis of a 75 g oral glucose tolerance test, using World Health Organization criteria (1985) [25]. Hemoglobin Alc (normal range 4%–6%) was measured to determine glycemic control. Beta-cell function was assessed by measuring plasma C-peptide in the fasting state, and at 30-minute intervals for 2 hours in response to 75 g oral glucose. Samples were collected on ice, and the plasma was stored at −70°C until the time of assaying. Pancreatic exocrine function was evaluated by measuring fasting serum trypsin (normal range 140–400 ng/ml) and fecal chymotrypsin (normal level > 8.3 U/g). The latter could be sampled in follow-up only in the intervention group. At the time of sampling all patients were pain-free and were off any enzyme supplements for at least a week.

Follow-up

All subjects were evaluated at 6-month intervals for clinical parameters and exocrine and β-cell function. For the purpose of the study, the data from the last patient follow-up visit were utilized for evaluation of results. Of the 14 subjects who underwent decompressive procedures, 1 patient died of unrelated hepatic failure 2 months after surgery, and 2 patients did not come for further evaluation on follow-up, despite numerous written reminders. Of the 11 patients on whom complete data were available, the median follow-up was 13 months (range 6–19 months), while in the 6 TCP patients who served as controls median follow-up was 10 months (range 8–12 months).

Assays

Plasma C-peptide was measured by radioimmunassay (Diagnostic System Laboratories, Webster, USA). The intra-assay and inter-assay coefficients of variation for the assay were 5% and 8.5%, respectively, and the limit of detectability was 0.3 nmol/l. Serum trypsin was measured by radioimmunassay (CIS Bio International, Gif-Sur-Yvette, France). The intra-assay and inter-assay coefficients of variation were 5% and 7.4%, respectively, and the limit of detectability was 8 ng/ml. Fecal chymotrypsin was detected by an enzymatic assay (Boehringer Mannheim, Mannheim, Germany). Intra- and inter-assay coefficients of variation were 3% and 7.5%, respectively. Hemoglobin Alc was determined by ion-exchange chromatography (Biorad, Richmond, USA).

Statistical Analysis

The results are expressed as mean ± SEM or median (interquartile range). For continuous variables, the Mann Whitney U test was used for comparison of independent groups, while the Wilcoxon signed-rank test was used for paired samples. Categorical variables were compared using the chi-square test or Fisher’s exact test. A two-tailed p value < 0.05 was considered significant.