

Pancreolauryl Test

Evaluation of a Tubeless Pancreatic Function Test in Comparison with Other Indirect and Direct Tests for Exocrine Pancreatic Function

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The sensitivity and specificity of the pancreolauryl test was evaluated in comparison with the NBT-PABA test, the estimation of fecal chymotrypsin and fat, and the secretin-pancreozymin test in 168 patients with and without pancreatic disease. The overall sensitivity rate was as follows: pancreolauryl test 90%, NBT-PABA test 86%, fecal chymotrypsin 66%. In patients with pancreatic steatorrhea the sensitivity of the pancreolauryl test was 100%, the NBT-PABA test 97%, and the fecal chymotrypsin estimation 92%. The specificity of these tests was: pancreolauryl test 97.6%, fecal chymotrypsin 87%, and NBT-PABA test 81.8%. The pancreolauryl test may be recommended as a noninvasive easy-to-perform tubeless pancreatic function test with a sufficiently high sensitivity and specificity.

Diagnosis of chronic pancreatitis is difficult (1). Since exocrine pancreatic function may be impaired before procedures such as ERCP, ultrasound, and computed tomography are able to demonstrate the presence of morphological changes and *vice versa* (2), it is necessary to test pancreatic function. However, direct tests such as the secretin-pancreozymin test or the Lundh test are time-consuming, invasive, unpopular with patients, and expensive. Therefore, indirect or tubeless pancreatic function tests have met increasing interest in recent years (3, 4).

The purpose of this prospective study was to evaluate the specificity and sensitivity of the pan-

creolauryl test (5, 6), the first oral pancreatic function test which has become available commercially, in comparison with other direct and indirect tests of exocrine pancreatic function.

MATERIALS AND METHODS

This comparative study was performed in 168 patients who were divided into the following groups:

Group 1. 60 healthy controls with no gastrointestinal disease.

Group 2. 41 patients with normal exocrine pancreatic function proven by the secretin-pancreozymin test. Final diagnoses in these cases were: recovery from acute pancreatitis ($N = 13$), irritable colon syndrome ($N = 8$), Crohn's disease ($N = 5$), celiac disease ($N = 3$), hyperlipoproteinaemia ($N = 3$), gastric resection (Billroth II), hiatus hernia, alcoholic hepatitis, liver cirrhosis, ileal resection, cholangitis, cholelithiasis, intraabdominal adhesions, and intestinal lymphangiectasis ($N = 1$ each).

Group 3. 60 patients with an abnormal secretin-pancreozymin test due to chronic relapsing pancreatitis, 35 (58.3%) of whom showed calcifications on plain abdominal x-rays. The etiology of chronic pancreatitis was alcoholism in 43 cases, but remained unknown in 15

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patients (25%). In 2 patients hereditary pancreatitis was suspected.

Group 4. 7 patients previously subjected to total pancreatectomy.

The following pancreatic function tests were performed.

Pancreolauryl Test (PLT). The test was performed in accordance with the instructions of the manufacturers (Temmler, Marburg, FRG). Briefly, the procedure was as follows: On the first day of the test fluorescein dilaurate is given orally in the middle of a standard breakfast which is used to stimulate the pancreas. Fluorescein dilaurate is hydrolyzed by arylesterases from the pancreas to release fluorescein which is readily absorbed from the gut, conjugated in the liver, and excreted in the urine (5). To enhance diuresis, the patient is asked to drink 1.5 liters of tea or mineral water. The test is repeated on the third day using free fluorescein only to correct the result for individual intestinal absorption, conjugation, and urinary excretion. Urinary fluorescein recovery over 10 hr is measured photometrically on both days. The recovery of the fluorescein on the test day (*T*) and the control day (*C*) is calculated and expressed as a *T/C* ratio: $T/C \text{ ratio} = (T/C) \times 100$.

According to the manufacturers' information a ratio of 30 and higher occurs with normal pancreatic function; a ratio below 20 indicates exocrine pancreatic insufficiency. If the ratio is between 20 and 30 the test must be repeated and is considered to be abnormal if the ratio is again in the same range.

NBT-PABA Test. In our test procedure 1 g NBT-PABA (Hoffmann-La Roche, Basle, Switzerland) was given with a Lundh test meal,* and urinary recovery of PABA was measured over 6 hr. The lower limit of normal for 6-hr PABA excretion was 50% of the dose given to healthy controls (7).

Fecal Chymotrypsin Estimation. Fecal chymotrypsin was kindly measured titrimetrically by Prof. R. Ammann, Zurich (8). Lower limit of normal is 120 $\mu\text{g/g}$ stool.

Fecal Fat Estimation. Fecal fat was analyzed in the majority of patients of group 3 according to van de Kamer et al (9). Steatorrhea was considered to be present if the daily stool fat excretion was above 7 g.

Secretin-Pancreozymin Test (SPT). This direct pancreatic function test was performed in all patients of groups 2 and 3 according to Creutzfeldt (10). In the fasted patient a double-lumen Lagerlöf tube is placed into the duodenum under x-ray control. Gastric secretion is discarded and duodenal secretion is collected at 15-min intervals. After 15 min of basal secretion, secretin (1 CU/kg body wt) and 30 min later cholecystokinin-pancreozymin (CCK-PZ; 1 IU/kg body wt) are given intravenously, while the patient is at rest on his right side. Both hormones were obtained from the Karolinska Institutet, Stockholm, Sweden. For evaluation of exocrine pancreatic function volume and bicarbonate concentration after stimulation with secretin and amylase, lipase and trypsin output after CCK-PZ were measured.

The exocrine pancreatic insufficiency was considered to be severe when bicarbonate concentration and enzyme output were reduced and to be slight to moderate when bicarbonate concentration was still normal, but when the output of only one or more enzymes was impaired (Table 1).

When the SPT and fecal fat results were combined, the following categories of pancreatic insufficiency were established: (1) slight, output of only one or more enzymes impaired; (2) moderate, bicarbonate concentration and enzyme output reduced, stool fat excretion still normal; and (3) severe, abnormal SPT result plus steatorrhea (Table 2).

RESULTS

Specificity. The *T/C* ratio of the PLT was well above 30 in all healthy controls.

The PLT was normal in all patients of group 2 except one (97.6%). This patient had had a Billroth II gastric resection and was suffering from gallstones. The PLT result was the same before and after cholecystectomy. During the SPT, the patient failed to show any contamination of the duodenal juice with bile after stimulation with CCK-PZ.

The NBT-PABA test was normal in 27 of 33 patients of this group (81.8%). Diagnoses of patients with a falsely abnormal result were irritable colon syndrome and recovery from acute pancreatitis (*N* = 2 in each case) as well as intestinal lymphangiectasis and liver cirrhosis (*N* = 1 in each case).

Fecal chymotrypsin was normal in 20 of 23 patients of group 2 (87%). The remaining patients suffered from hiatus hernia, liver cirrhosis, and recovery from acute pancreatitis.

Sensitivity. In patients with chronic relapsing pancreatitis (group 3) test results were correctly abnormal as follows: with the PLT in 54 of 60 (90%), NBT-PABA test 51 of 59 (86%), fecal chymotrypsin 36 of 54 patients (66%).

When patients were divided into groups in accordance with their SPT result (Table 1), correctly abnormal fecal chymotrypsin figures went up to 86% in severe exocrine pancreatic insufficiency, but still failed to reach the level of the oral pancreatic function tests. In the less severely impaired patients, the latter tests were distinctly superior to stool enzyme estimation.

When compared with the combined results of SPT and fecal fat analysis, the sensitivity of all indirect tests was comparable when exocrine pancreatic insufficiency was severe, ie, when steatorrhea was present. In patients with slight to moder-

*300 ml Spontafix®: Fresenius, Bad Homburg v.d.H., FRG; 3.6% fat; 4% protein; 14.7% carbohydrates.

TABLE 1. INDIRECT PANCREATIC FUNCTION TESTS COMPARED TO SECRETIN-PANCREOZYMIN TEST (SPT)

	PLT		NBT-PABA test		Fecal chymotrypsin	
	N	Abnormal	N	Abnormal	N	Abnormal
Bicarbonate concentration normal*	20	15 = 75%	19	14 = 79%	19	6 = 32%
Enzyme output abnormal†						
Bicarbonate concentration and enzyme output abnormal	40	39 = 98%	40	37 = 93%	35	30 = 86%

*Maximal concentration of bicarbonate: >70 mVal/liter (normal).

†Amylase, trypsin, and lipase output 30 min after CCK-PZ: > $\bar{X} \pm 2$ SD of healthy controls; amylase output 28,000 \pm 16,000 units/30 min ($\bar{X} \pm 2$ SD); trypsin output 60 \pm 30 units/30 min; lipase output 130,000 \pm 65,000 units/30 min.

ate insufficiency, both oral function tests were again superior to fecal enzyme estimation (Table 2).

Before investigating patients previously subjected to total pancreatectomy, pancreatic enzyme substitution was discontinued for 5 days; chymotrypsin was virtually not detectable in the stools. Figures for T/C ratio were between 1.9 and 7.8, and PABA excretion was between 0% and 22.4%.

DISCUSSION

Since most patients in this study were transferred to our department suspected of suffering from chronic pancreatitis, the incidence of this disease was indeed very high. Therefore our data on the specificity of the tests are based on a preselected group of patients. Bearing this reservation in mind, we have found the PLT to be more specific than fecal chymotrypsin estimation and the NBT-PABA test. However, the specificity of the latter may be improved by using free PABA alone (11).

The only falsely abnormal PLT was observed in a patient with prior gastric resection (Billroth II) and

a gallbladder that was obviously not functioning well. It is conceivable that this result is due to a postprandial asynchrony so that pancreatic juice did not reach the test capsules in time. However, there are some inexplicable PLT results in patients with bile-pancreatic juice admixture problems (12).

The overall sensitivity of the PLT was also satisfactory, especially in patients with moderately or severely impaired pancreatic function. In patients with overt pancreatic failure (steatorrhea) none had a falsely normal test result. In this group of patients the sensitivity of the other tests was also excellent.

Data for the NBT-PABA test and fecal chymotrypsin are in the same range as found previously in a prospective study by this laboratory (7).

The data are in accordance with those of another comparative study involving a smaller group of patients (13) with the exception that in this investigation chymotrypsin results showed a higher sensitivity. Furthermore, the PLT results of the present study are slightly worse than in the original study of Kaffarnik et al (6). However, pancreatic function was not always well documented in these patients.

TABLE 2. INDIRECT PANCREATIC FUNCTION TESTS COMPARED TO SECRETIN-PANCREOZYMIN TEST (SPT) AND FECAL FAT ESTIMATION IN PATIENTS OF GROUP 3 IN WHOM LATTER TESTS WERE PERFORMED

SPT	PLT		NBT-PABA test		Fecal chymotrypsin	
	N	Abnormal	N	Abnormal	N	Abnormal
Bicarbonate concentration normal*						
Enzyme output abnormal†	16	11 = 67%	15	11 = 73%	16	4 = 25%
Fecal fat normal‡						
Bicarbonate concentration and enzyme output abnormal	8	7 = 88%	8	7 = 88%	5	3 = 60%
Fecal fat normal						
Bicarbonate concentration and enzyme output abnormal	29	29 = 100%	29	28 = 97%	26	24 = 92%
Steatorrhea						

*Normal maximal concentration of HCO₃ > 70 mval/liter after secretin.

†Normal amylase, trypsin, and lipase output after CCK-PZ > $\bar{X} \pm 2$ SD of healthy controls; amylase output 28,000 \pm 16,000 units/30 min ($\bar{X} \pm 2$ SE); trypsin output 60 \pm 30 units/30 min; lipase output 130,000 \pm 65,000 units/30 min.

‡Normal stool fat < 7 g/day.

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The results obtained in patients previously subjected to total pancreatectomy are difficult to explain. An intact absorption of NBT-PABA has been demonstrated *in vitro* and *in vivo* (14, 15). Future studies will have to show whether there is a non-pancreatic hydrolysis of fluorescein dilaurate. Recently it has been shown that some bacteria (streptococci) are able to hydrolyze fluorescein dilaurate (16), and the results obtained in our patients may be due to bacterial overgrowth after total pancreatectomy. It is of interest that chymotrypsin-like activity of some bacteria, possibly leading to falsely normal NBT-PABA test results, has been reported (17).

On the basis of this study the following conclusions may be drawn: While the PLT will not replace the SPT or the Lundh test, this noninvasive, easy-to-perform tubeless pancreatic function test may be used at places where direct methods are not available. The test has a sufficiently high specificity and sensitivity. An abnormal test result indicates exocrine pancreatic insufficiency in patients without gastric resection and biliary disease. A normal PLT result excludes moderate to severe exocrine pancreatic impairment. Furthermore, the test seems to be useful not only in adults, but may also be used successfully in children (18).

However, similar to all pancreatic function tests, the PLT is unfortunately unable to differentiate between pancreatic insufficiency due to chronic pancreatitis and that due to pancreatic cancer.

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