Evaluation of an extended pancreatic function test in normal subjects and in patients with chronic pancreatitis

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Summary

Exocrine pancreatic response was evaluated in patients with varying degrees of pancreatic damage and in control subjects by means of an extended pancreatic function test (PFT). A second injection of secretin and pancreozymin was given after completion of the standard test. The discriminatory value of the standard PFT with regard to bicarbonate and enzyme output was not enhanced by a second bolus dose of hormones. It is concluded that the secretory potential of damaged pancreatic exocrine tissue cannot be exhausted by prolonged stimulation employing repeat bolus stimulation.

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Tests based on secretory function usually reflect structural changes in the pancreas. These include the use of exogenous hormones, the Lundh meal and an oral pancreatic function test (PFT) utilizing a synthetic peptide.[1-5] Although stimulation of exocrine pancreatic secretion with hormonal preparations has been shown to be the most sensitive method of detecting mild degrees of pancreatic dysfunction,[6,7] there is still no uniform methodology for performing the test.[8,9] Since an overlap exists between control and disease groups, investigators have tried to increase the discriminatory value of these tests by prolonged stimulation of the pancreas. It has been claimed that this may enhance differences between normal and pathological responses.[10]

We have therefore examined the role of an extended PFT in an attempt to accentuate slight differences in the pancreatic exocrine response to exogenous stimulants in patients with varying degrees of pancreatic damage and control subjects.

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Patients and methods

Twenty patients being investigated for chronic pancreatitis were studied. There were 7 subjects with chronic calcific pancreatitis (CCP) (mean age 43,4 years, range 29-56 years) and 7 with non-calcific chronic pancreatitis (NCP) (mean age 48,7 years, range 31-71 years). Diagnoses were confirmed in all cases by the clinical history, an abnormal response to a standard secretin-pancreozymin test, endoscopic retrograde cholangiopancreatography and computed tomography. There were 6 subjects (mean age 45,6 years, range 26-56 years) in whom a diagnosis of chronic pancreatitis could not be substantiated by the above methods. Final diagnoses in the latter 6 subjects (who formed our control group) were peptic ulcer disease (3 patients), irritable bowel syndrome (2 patients) and cholelithiasis (1 patient).

After an overnight fast two Salem sump tubes (Argyle) were passed via the nasogastric route. Under fluoroscopic control, one tube was positioned in the distal second part of the duodenum and the other in the dependent part of the stomach for continual aspiration of gastric contents. Following a 10-minute basal col-

lection, which was discarded, an intravenous bolus of secretin 2 U/kg (Boots, batch No. 91510/4) was given and the duodenal contents were aspirated for six consecutive 10-minute periods. After 1 hour an intravenous bolus of pancreozymin 1,5 U/kg (Boots, batch No. 91331/2) was given and a further two 10-minute collections were made. This constituted our standard PFT. A second similar dose of the same batch of secretin and pancreozymin was given simultaneously 30 minutes after termination of the PFT and duodenal aspirate collected for a further 20 minutes. This constituted the extended PFT.

The bicarbonate, trypsin, chymotrypsin, amylase and lipase concentrations and output of each sample were analysed by methods previously described,[3] and volumes were noted. All samples were analysed on the same day as the test. For the purpose of this study the pooled final 20-minute collection of the standard PFT (test 1) was compared with the 20-minute collection of the extended PFT (test 2).

The differences between test 1 and test 2 for the various groups were compared by an analysis of variance. Means were compared using contrast coefficients.

Results

As expected, the mean values for all modalities tested were higher in the control group and the mean levels of the patients with CCP were lower than those of patients with lesser degrees of pancreatic damage. Six of the 7 patients with NCP had an only mildly abnormal standard PFT, with not more than 2 of 7 parameters (volume, maximal bicarbonate concentration, mean concentrations of bicarbonate, amylase, trypsin, chymotrypsin and lipase) abnormal.

The mean values for all modalities in the CCP group were so low that minor fluctuations resulted in large percentage changes. It was therefore decided that more meaningful data might be obtained by comparing the NCP patients (the group with a lesser degree of pancreatic damage) with the control subjects rather than by combining the CCP and NCP groups.

Volume and bicarbonate and enzyme concentrations

The mean enzyme concentrations were somewhat lower in repeat tests in both the NCP and the control groups (Table I). The decrease in mean amylase, trypsin and chymotrypsin concentrations tended to be more marked in the NCP group than in the control group, but significance was attained only with regard to the relative differences in mean trypsin concentrations ($P < 0,05$). The mean volume of pancreatic secretion tended to increase after repeat tests in all groups.

Bicarbonate and enzyme output

There were no significant differences between the mean output of bicarbonate, amylase, lipase, trypsin and chymotrypsin in the groups (Table II).

Discussion

The possibility of being able to exhaust the pancreatic flow of enzymes by prolonged stimulation is particularly attractive when one is attempting to distinguish minimal or early pancreatic dysfunction from normal function.

Data from this laboratory have shown that the results of tandem secretin-cholecystokinin tests carried out after an interval of 30 minutes gave reproducible pooled results.[11] However,

TABLE I. VOLUME, BICARBONATE AND ENZYME CONCENTRATIONS (MEAN ± SE)

	Test 1	Test 2	% change in means
Volume (ml/20 min)			
CCP ($N = 7$)	**46 ± 9,2**	**57 ± 7,2**	
NCP ($N = 7$)	**85 ± 6,8**	**119 ± 10,1**	**+40%***
Controls ($N = 6$)	**117 ± 14,8**	**142 ± 25,0**	**+21%**
Bicarbonate (mEq/l)			
CCP	**38 ± 8,4**	**43 ± 8,4**	
NCP	**80 ± 8,0**	**75 ± 6,0**	**-6%****
Controls	**81 ± 4,0**	**81 ± 4,7**	**0%**
Amylase (x 10^3 U/ml)			
CCP	**1,9 ± 1,05**	**1,6 ± 0,85**	
NCP	**7,3 ± 2,76**	**5,3 ± 1,89**	**-22%***
Controls	**10,8 ± 1,66**	**10,3 ± 1,43**	**-5%**
Lipase (x 10^3 IU/l)			
CCP	**111 ± 34**	**139 ± 40**	
NCP	**495 ± 85**	**430 ± 83**	**-13%****
Controls	**758 ± 103**	**626 ± 79**	**-17%**
Trypsin (BAEE U/ml)			
CCP	**954 ± 332**	**1 093 ± 371**	
NCP	**4 087 ± 557**	**3 250 ± 519**	**-20%***
Controls	**6 203 ± 558**	**6 016 ± 1 031**	**-3%**
Chymotrypsin (ATEE U/ml)			
CCP	**595 ± 266**	**827 ± 451**	
NCP	**3 553 ± 632**	**2 696 ± 287**	**-24%****
Controls	**4 469 ± 543**	**4 108 ± 507**	**-8%**

* $P < 0,05$ compared with control value.
** Not significantly different from control value.
BAEE = *N*-benzoyl-L-arginine ethyl ester; ATEE = *N*-acetyl-L-tyrosine ethyl ester.

TABLE II. BICARBONATE AND ENZYME OUTPUTS (/20 MIN) (MEAN ± SE)

	Test 1	Test 2
Bicarbonate (mEq)		
CCP ($N = 7$)	2,0 ± 0,66	2,5 ± 0,56
NCP ($N = 7$)	6,8 ± 0,60	9,2 ± 1,01
Controls ($N = 6$)	9,3 ± 1,91	11,0 ± 2,31
Amylase (x 10^3 U)		
CCP	88 ± 48,27	82 ± 40,26
NCP	604 ± 200,45	598 ± 162,55
Controls	1 272 ± 284,96	1 432 ± 316,89
Lipase (x 10^3 IU)		
CCP	5,5 ± 1,81	7,6 ± 2,10
NCP	41,8 ± 6,50	49,1 ± 7,44
Controls	87,4 ± 15,68	83,6 ± 14,65
Trypsin (BAEE U)		
CCP	45 770 ± 13 380	55 400 ± 14 870
NCP	345 170 ± 57 060	366 560 ± 50 240
Controls	714 040 ± 83 930	706 640 ± 58 920
Chymotrypsin (ATEE U)		
CCP	27 140 ± 9 830	39 330 ± 16 960
NCP	299 240 ± 62 770	313 620 ± 33 300
Controls	538 180 ± 107 300	536 440 ± 86 090

BAEE = *N*-benzoyl-L-arginine ethyl ester; ATEE = *N*-acetyl-L-tyrosine ethyl ester.

these data were obtained in a large number of patients with a variety of diseases. No attempt was made to assess whether patients with varying degrees of pancreatic damage responded differently from other patients studied.

The results obtained in the present study with a bolus injection do not necessarily imply that a difference might not occur with constant infusion.[10] Although in the present study there was a tendency for bicarbonate, amylase, trypsin and chymotrypsin concentrations to be lower following repeat bolus stimulation in the patients with NCP than in the controls, there may have been a dilutional effect caused by the increased volume following such stimulation. There was, however, no difference with regard to enzyme output, a finding in keeping with the observations of Dreiling *et al.*[12] These workers demonstrated increases in volume, bicarbonate and amylase output in patients with chronic pancreatitis and in controls when a large bolus dose of secretin was repeated 80 minutes after a smaller dose.

There is no uniformity in the literature regarding the preparation or sequence or mode of administration of exogenous hormones with regard to testing of pancreatic function. The same applies to attempts to discriminate early pancreatic dysfunction from normal function by prolonged stimulation, in the hope of exhausting the pancreatic flow of enzymes in the former group. Unfortunately, techniques in the few reported studies of this type have differed. In addition it has not yet been demonstrated that the response of the normal and/or diseased pancreas to repeat bolus injections and constant infusion is similar. It is possible, therefore, that the differences in results obtained are caused by the different techniques employed.

The rates of synthesis of pancreatic enzymes in health and disease have not been directly measured, and it is not known whether the secretory ability of the cells in the diseased pancreas is any different from that of the cells in the normal gland. However, the findings in the present study suggest that the secretory potential of surviving acinar cells in patients with chronic pancreatitis is comparable to that of acinar cells in normal control subjects. If correct, this hypothesis suggests that the differences in capacity to secrete enzymes represent a decrease in the mass of pancreatic acinar tissue and may explain the failure of repeat bolus injection to accentuate differences between patients with chronic pancreatitis and controls with regard to enzyme secretion.

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REFERENCES

1. Marks IN, Tompsett SL. The diagnosis of pancreatic disease with special reference to a test of pancreatic secretion utilizing both secretin and pancreozymin stimulation. *Q J Med* 1958; **27:** 431-461.
2. Burton P, Evans DG, Harper AA *et al.* A test of pancreatic function in man based on the analysis of duodenal contents after administration of secretin and pancreozymin. *Gut* 1960; **1:** 111-124.
3. Bank S, Marks IN, Moshal MG, Efron G, Silber R. The pancreatic function test — method and normal values. *S Afr Med J* 1963; **37:** 1061-1066.
4. James O. The Lundh test. *Gut* 1973; **14:** 582-591.
5. Arvanitakis C, Greenberger NJ. Diagnosis of pancreatic disease by a synthetic peptide: a new test of exocrine pancreatic function. *Lancet* 1976; **i:** 663-666.
6. Lurie B, Brom B, Bank S, Novis B, Marks IN. Comparative response of exocrine pancreatic secretion following a test meal and secretin-pancreozymin stimulation. *Scand J Gastroenterol* 1973; **8:** 27-32.
7. Gyr K, Agrawal NM, Felsenfeld O, Font RG. Comparative study of secretin and Lundh tests. *Am J Dig Dis* 1975; **20:** 506-512.
8. Arvanitakis C, Cooke AR. Diagnostic tests of exocrine pancreatic function and disease. *Gastroenterology* 1978; **74:** 932-948.
9. Wormsley KG. Tests of pancreatic secretion. *Clin Gastroenterol* 1978; **7:** 529-544.
10. Gullo L, Costa PL, Labo G. Investigation of exocrine pancreatic function by continuous infusion of caerulein and secretin in normal subjects and in chronic pancreatitis. *Digestion* 1976; **14:** 97-107.
11. Clain J, Bank S, Barbezat GO, Novis BH, Marks IN. A comparison between secretin alone and sequential and simultaneous secretin and cholecystokinin administration in the assessment of pancreatic function. *Gut* 1974; **15:** 885-888.
12. Dreiling DA, Greenstein AJ, Bordalo O. Comparison of standard and augmented secretin test responses in patients with and without pancreatic disease. *Am J Gastroenterol* 1974; **61:** 433-442.