

# Faecal elastase-1: helpful in analysing steatorrhoea?

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## ABSTRACT

**Background:** The faecal elastase-1 test (FE-1) is considered easy to perform and sensitive to detect severe and moderate exocrine pancreatic insufficiency. However, little information is available on the specificity of this test in the analysis of steatorrhoea. Our aim was to evaluate the clinical value of FE-1 in the analysis of patients sent in for faecal fat determination.

**Methods:** Stool samples were collected over 24 hours in 40 healthy controls and 119 patients: 58 patients with chronic pancreatitis and 61 nonpancreatic disease patients with chronic diarrhoea. Faecal fat excretion was determined and FE-1 was measured using a commercially available ELISA kit, which employs two monoclonal antibodies to bind to two distinct epitopes of human pancreatic elastase-1.

**Results:** Faecal elastase-1 test shows good reproducibility. The test lacks sensitivity in detecting exocrine pancreatic insufficiency and chronic pancreatitis (68 and 59%, respectively). However, it is specific with respect to differentiating pancreatic from nonpancreatic causes in patients with steatorrhoea.

**Conclusion:** FE-1 lacks sensitivity to detect chronic pancreatitis. It can serve as a simple, noninvasive method to determine the aetiology of steatorrhoea.

## INTRODUCTION

For evaluation and follow-up of exocrine pancreatic function, several tests are available.<sup>1</sup> The secretin-cholecystokinin test (SCT) is considered the gold standard. However, this test requires duodenal intubation, is time consuming, expensive and lacks standardisation. Its use, therefore, is limited to research purposes. Indirect tests either determine

the amount of unabsorbed nutrients in the stool (i.e. faecal fat excretion) or measure directly or indirectly the enzyme activity in blood, stool, urine or breath.<sup>2</sup> These procedures are relatively easy to perform, while discomfort is limited. The indirect tests lack sensitivity in mild and moderate exocrine pancreatic insufficiency, and their specificity is questionable. Some years ago the faecal elastase-1 test was introduced. This test is considered specific for human pancreatic elastase so that exogenous enzyme supplements do not affect the test result.<sup>3</sup> Elastase-1 concentration in faeces is about five times higher than in pancreatic juice, illustrating its stability during intestinal transport.<sup>4</sup> Several studies have compared faecal elastase-1 with other indirect and direct tests in pancreatic disease but varying and contrasting results have been obtained. With steatorrhoea, it is relevant to distinguish between pancreatic and other gastrointestinal causes. Despite extensive data on faecal elastase output in patients with chronic pancreatitis, little is known on the specificity of the faecal elastase test.<sup>5-11</sup>

The aim of our study was to evaluate the clinical value of faecal elastase-1 in patients with chronic pancreatitis and in patients with chronic diarrhoea with or without fat malabsorption due to nonpancreatic gastrointestinal disorders. In steatorrhoea patients we tested the ability of faecal elastase-1 to distinguish between pancreatic and nonpancreatic aetiologies.

## MATERIALS AND METHODS

### Patients

Between 1996 and 2000, stools sent in for faecal fat determination were also analysed for faecal elastase-1

concentration. The study group consisted of 119 patients with a mean age of 49 (range 17 to 75 years), 57 male and 62 female. In the patients with chronic pancreatitis, the diagnosis was based on clinical history, morphological changes seen on ultrasonography and/or CT scan, and endoscopic retrograde cholangiopancreatography (ERCP). An elevated faecal fat excretion (a sign of decompensated exocrine pancreatic insufficiency) was present in 38 of the 58 chronic pancreatitis patients. Sixty-one patients with chronic diarrhoea due to nonpancreatic gastrointestinal disorders were included. They consisted of patients with gastrectomy (n=11), systemic sclerosis (n=4), inflammatory bowel disease (n=20) and functional diarrhoea (n=26) patients. All had symptoms of frequent bulky stools and/or diarrhoea, and 30 patients had steatorrhoea. We included 40 healthy controls (mean age 27, range 16-74 years, even gender distribution) who had no history of gastrointestinal or pancreatic disease and had a normal faecal fat excretion (<7 g/24 h). The effect of exogenous enzyme supplements (mean dosage 3 x 25,000 IU lipase) on faecal elastase-1 was assessed in 13 chronic pancreatitis patients. Repeatability was tested in a group of 46 individuals (31 healthy controls, 10 chronic pancreatitis patients and 5 nonpancreatic disease patients). Faecal elastase-1 was determined in stools that were collected over 24 hours on two consecutive days.

#### Methods

Stools were collected over a 24-hour period while the subject was on a standard diet with a mean daily fat intake of around 100 g. Quantitative fat was determined using the Van de Kamer method. Faecal elastase-1 was measured using an enzyme-linked immunosorbent assay (ELISA kit available from ScheBo-Tech, Giessen, Germany) employing two monoclonal antibodies binding to two distinct epitopes of human pancreatic elastase.<sup>12</sup> In each (24-hour) stool collection, faecal elastase concentration and faecal fat excretion were analysed.

#### Analysis

The cut-off value for faecal elastase-1 was defined as the mean value in the control group minus twice the standard deviation. Two series of data did not exhibit a normal distribution, namely the chronic pancreatitis group with exocrine insufficiency and a subgroup of the nonpancreatic disease patients (gastrectomy). To be able to apply a parametric statistical model, raw data were transformed by means of the square root method. Statistical differences were analysed using a one-way analysis of variance model (SPSS), contrasts were defined as being significant at  $p=0.05$  or less. Sensitivity and specificity of the faecal elastase-1 test for detecting exocrine pancreatic insufficiency were calculated. The data of the faecal elastase and the faecal fat excretion used to assess the influence of exogenous

enzyme did not show a normal distribution, so the non-parametric Wilcoxon signed-rank test was used. The two consecutive faecal elastase values obtained from the healthy volunteers did not exhibit a normal distribution either. Repeatability was therefore analysed using the Wilcoxon signed-rank test. The coefficients of variation and the standard deviation of the measurement error were calculated.

## RESULTS

Clinical and biochemical data of the patients with chronic pancreatitis are given in *table 1*. The cut-off value for faecal elastase-1 based on our healthy volunteer population was calculated to be 218  $\mu\text{g/g}$  faeces. *Table 2* shows the results of all the faecal elastase and fat excretion data. Of the chronic pancreatitis patients with steatorrhoea, 26 had a reduced but 12 had a normal faecal elastase-1 concentration. As for the chronic pancreatitis patients with compensated exocrine pancreatic insufficiency (no steatorrhoea), 12 had normal and eight had low faecal elastase-1 concentrations. In the nonpancreatic disease patient group, all but five had normal faecal elastase-1 concentrations. Of these five, four had undergone a gastrectomy and one patient had Crohn's disease. The faecal elastase-1 concentrations in the chronic pancreatitis group with steatorrhoea were significantly ( $p<0.001$ ) lower than those in the chronic pancreatitis group without steatorrhoea. The entire chronic pancreatitis group had significantly ( $p<0.001$ ) lower faecal elastase-1 concentrations compared with nonpancreatic

**Table 1**  
*Clinical and biochemical data on patients with chronic pancreatitis (CP)*

	CP WITH STEATORRHOEA (N=38)	CP WITHOUT STEATORRHOEA (N=20)
Aetiology of CP		
- Alcohol	19 (50%)	9 (45%)
- Idiopathic	14 (37%)	10 (50%)
- Hereditary	3 (8%)	
- Pancreas divisum	1 (3%)	1 (5%)
- Hypercalcaemia	1 (3%)	
Duration of CP (years) mean, range	5.5 (0.3-25)	4.3 (0.3-13)
Serum amylase (u/l) mean, range	140 (32-237)	182 (61-312)
Weight loss (kg) mean, range	2.3 (0-10)	1.8 (0-17)
Endocrine insufficiency:		
- Impaired glucose tolerance	4 (11%)	6 (30%)
- Insulin dependent	13 (34%)	3 (15%)

**Table 2**

Data on faecal fat excretion determination and faecal elastase-1 estimation in healthy controls, chronic pancreatitis patients and nonpancreatic chronic diarrhoea patients (cut-off value is 218 µg/g faeces)

GROUP	NO. OF PATIENTS	MEAN 24 H FAECAL FAT EXCRETION (± SEM)	MEAN FAECAL ELASTASE-1 CONCENTRATION (± SEM)	NO. (%) WITH FAECAL ELASTASE-1 <218 µG/G
Healthy controls	40	3.4 ± 1.4	636.1 ± 33.1	1 (2.5%)
Chronic pancreatitis	58	16.3 ± 2.6	200.3 ± 28.5	34 (59%)
With steatorrhoea	38	22.5 ± 3.7	145.8 ± 31.2	26 (68%)
Without steatorrhoea	20	4.5 ± 0.4	303.8 ± 52.1	8 (40%)
Nonpancreatic disease patients	61	11.2 ± 1.4	568.6 ± 36.2	5 (8.2%)
With steatorrhoea	31	18.2 ± 2.1	552.9 ± 50.4	3 (9.7%)
Without steatorrhoea	30	3.8 ± 0.3	595.9 ± 49.6	2 (6.7%)

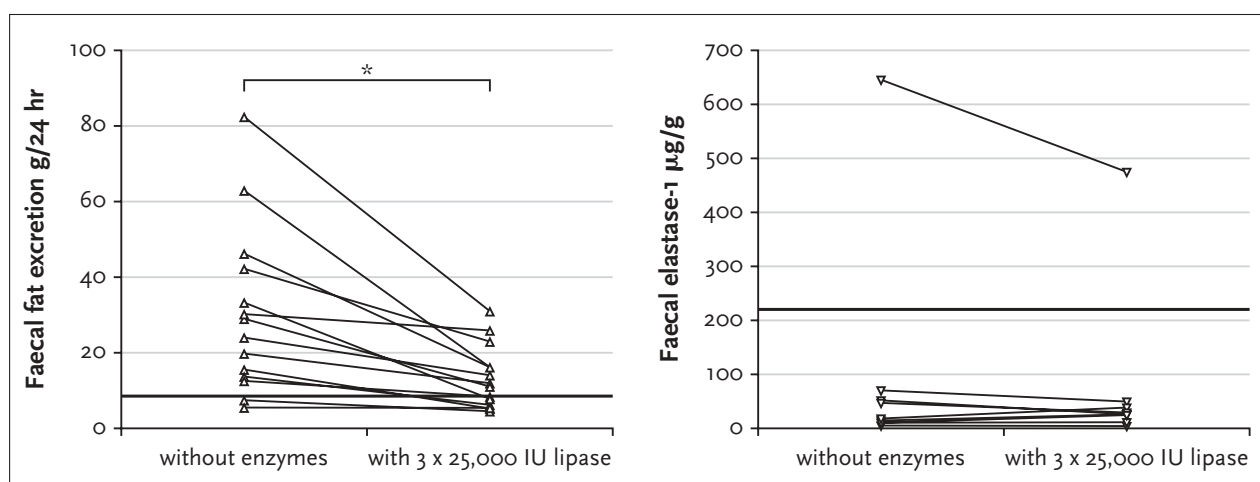
disease patients. There were no statistically significant differences between nonpancreatic disease patients and healthy controls. The sensitivity of the faecal elastase-1 concentrations was 68% for detecting decompensated exocrine pancreatic insufficiency in patients with chronic pancreatitis. The specificity for chronic pancreatitis was calculated to be 93% for the entire chronic pancreatitis group. Our aim was to evaluate the usefulness of faecal elastase-1 in steatorrhoea. Therefore we grouped the patients (n=69) with an elevated faecal fat excretion of all aetiologies. Of these 69 patients, 29 had a positive faecal elastase-1 test (concentration below 218 µg/g): 90% (26) were chronic pancreatitis patients and 10% (3) gastrectomy patients.

Figure 1 shows the effect of exogenous enzyme supplements on faecal elastase concentration and fat excretion. After seven days of enzyme supplement therapy the faecal fat excretion was significantly reduced (p=0.002 compared with basal) but faecal elastase output did not significantly change.

As for repeatability, there was a strong correlation between the faecal elastase value on the first and second day of stool collection (p=0.921). The mean coefficient of variation was 15.7% and the standard deviation of the measurement error was 124.4.

## DISCUSSION

Previous studies on the faecal elastase-1 test have shown promising results. Faecal elastase-1 concentration is about five- to six-fold the duodenal concentration and hardly influenced by motility disorders or mucosal defects.<sup>8</sup> As the assay determines concentration, only a single sample of a stool is required. The assay is specific for human elastase suggesting that it is not necessary to discontinue exogenous enzyme supplementation previous to stool sampling, as was confirmed by our data. In our healthy volunteers we determined a cut-off value (218 µg/g) for



**Figure 1**

Effect of exogenous enzyme supplements on faecal fat excretion and faecal elastase concentration in 14 chronic pancreatitis patients of which 12 with steatorrhoea (faecal fat excretion > 7 g/24 h). Faecal fat excretion decreased from 30 g/24 h to 13 g/24 h (p=0.002; indicated by \*). Faecal elastase before and during exogenous enzyme use is not affected by exogenous enzyme supplementation.

faecal elastase, which is comparable with the suggested cut-off by the manufacturer and with results from other studies.<sup>3,6</sup>

Although the faecal elastase concentrations in the chronic pancreatitis group with steatorrhoea were significantly lower than in the chronic pancreatitis patients without steatorrhoea and the nonpancreatic disease controls, the sensitivity compared with faecal fat analysis was poor. Of all chronic pancreatitis patients, 41% had a faecal elastase >218 µg/g. In the chronic pancreatitis group with steatorrhoea, there were still 35% with a normal faecal elastase-1. Our findings certainly do not confirm the high sensitivities reported by others<sup>6-8,12</sup> and are more in accordance with the work by Lankisch *et al.* reporting 82% true-positives of the faecal elastase-1 test in severe exocrine pancreatic insufficiency, but less than 50% in mild and moderate insufficiency. These authors used a functional classification based on the secretin-cholecystokinin test and faecal fat excretion.<sup>13</sup> Amann *et al.* came to the same conclusion (low sensitivity of 40%) but their results were obtained in a group of 14 chronic pancreatitis patients.<sup>14</sup>

Hardt *et al.* reported sensitivities of 45% for faecal elastase-1 in predicting the presence of ductal changes in a large group of patients undergoing ERCP.<sup>11</sup>

Of the patients with steatorrhoea that we analysed, 42% had a faecal elastase concentration below 218 µg/g. Of these patients, 90% had chronic pancreatitis with exocrine pancreatic insufficiency. The three false-positives (patients with steatorrhoea without pancreatic disease) consisted of patients after partial gastrectomy. None of the gastrectomy patients had any evidence of pancreatic disease (normal morphology confirmed by ultrasonography or CT scan) or a history of pancreatic symptoms. In fact four out of five false-positive test results in the nonpancreatic disease patient group were gastric resection patients, three of whom had steatorrhoea. It has been suggested that the presence of dumping symptoms, with rapid intestinal passage and voluminous stools may lead to dilution and a subsequent lower faecal elastase concentration in the stool sample. In an attempt to explain low elastase concentrations in patients with nonpancreatic malabsorption, Amann *et al.* also suggested that liquid stool may perturb accurate determination.<sup>14</sup> This does not explain the results in our gastrectomy patients as the mean faecal mass was 245 g/24 h, which is equal to the 244 g/24 h in the rest of the nonpancreatic disease control patients with a normal faecal elastase-1. Another factor to explain low faecal elastase levels in patients after gastric surgery may be a disturbance in the neurohormonal signals that stimulate exocrine pancreatic secretion.<sup>15</sup>

We prospectively collected data on faecal elastase-1 concentration in stools from patients sent to our laboratory for faecal fat analysis. Based on this cohort of nonselected

patients we evaluated the potential clinical value of the faecal elastase-1 test. It is concluded that the faecal elastase-1 test shows good reproducibility. The test lacks sensitivity in detecting exocrine pancreatic insufficiency and chronic pancreatitis. However, the test is specific with respect to differentiating pancreatic from nonpancreatic causes in patients with steatorrhoea.

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