Fecal Elastase 1 ELISA For Exocrine Pancreatic Insufficiency: Comparison With ERCP-Morphology And Fecal Fat Excretion

Hardt P.D., Nalop J., Marzeion A.M., Kloer H.U.

Third Medical Department, University Hospital, Giessen, Germany

Introduction

The measurement of fecal elastase 1 concentrations (FEC) using an ELISA based on monoclonal antibodies has become a popular test of exocrine pancreatic function. It had initially been evaluated in comparison with direct function tests showing good sensitivity and specificity in moderate to severe exocrine dysfunction [1,2]. When this test became available first, it was criticized for low sensitivity in mild pancreatitis. Later, when it was widely used because of being superior to other indirect function tests, FEC measurement was doubted to be specific, because a lot more pathological results were obtained than suspected according to traditional theories on chronic pancreatic disease [3,4]. As in any other fecal test false results due to dilution must be considered. In our experience this is usually not of clinical relevance exept in watery stools. It has been shown, that elastase 1 levels can be reduced in duodenal disease and that they are normalized after successful treatment [5]. However, in most of the cases, reduced levels seem to represent exocrine dysfunction. In this present study we compared FEC to ERCP morphology, the gold standard of imaging and we investigated fecal fat excretion (FFE) in patients with pathological FEC to learn more about the implications of reduced FEC.

Methods

Fecal elastase 1 measurement

FEC was measured using the ELISA provided by ScheBo Biotech AG, Giessen, Germany. Concentrations > 200 µg/g were regarded as normal, 51-200 were regarded as mild insufficiency and levels < 50 µg/g were regarded as severe exocrine insufficiency.

1. ERCP study

ERCP-images of 213 consecutive patients investigated for different reasons were reevaluated concerning pancreatic duct morphology. Duct findings were classified normal or chronic pancreatitis grade I-III according to the Cambridge-classification. In all patients FEC had been measured at the time of ERCP performance. FEC and ERCP data were compared.

2. Fecal fat excretion (FFE) study

Patients with FEC < 100 µg/g were on a diet including a minimum oral fat intake of 100 g/day for 4 days followed by complete stool sampling during the last 72 hrs. Fecal fat excretion was measured using the method described by Van de Kamer. FFE < 7 g/day was considered as normal. Dietary fat intake and clinical symptoms were recorded in standard questionnaires. Patients with any known reason for fat maldigestion (e.g. GI-surgery) were excluded from the study.

Figure 1: Fecal elastase 1 concentrations depending on the grade of morphological changes

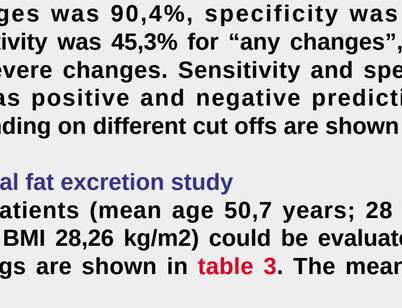

Table 1: Exocrine Insufficiency according to fecal elastase 1 measurements depending on the grade of morphological changes

Pancreatic duct findings	Normal	Mild changes CP°I	Moderate changes CP°II	Severe changes CP°III
Normal exocrine Function E1>200 µg/gl	9	47	51	12
Mild exocrine Insufficiency E1 51-200 µg/g	1	5	32	17
Severe exocrine Insufficiency <50 severe	2	1	14	22

p<0,01; CP=chronic Pancreatitis

Results

1. ERCP study

There was a significant correlation between FEC and pancreatic duct changes (see figure 1 and table 1). Using a cut off point of 200 µg/g the positive predictive value of FEC for moderate+severe duct changes was 90,4%, specificity was 86%. The sensitivity was 45,3% for “any changes”, but 76,5% for severe changes. Sensitivity and specificity, as well as positive and negative predictive values depending on different cut offs are shown in table 2

2. Fecal fat excretion study

101 patients (mean age 50,7 years; 28 female, 73 male, BMI 28,26 kg/m2) could be evaluated. Clinical findings are shown in table 3. The mean fat intake was 118,87 g/d, the mean fat excretion was 9,19 g. Only 41 patients (40,6%) had normal fat excretion < 7 g/d. It was moderately increased (7-10 g/d) in 20 patients (19,8%) (figure 2). In 40 patients (39,6%) it was higher than 10 g/d, in 12 > 15 g/d. The mean coefficient of fat absorption (CFA) was reduced to 91,79%. Fat excretion did not correlate with clinical findings.

Table 2: Sensitivity, Specificity, positive predictive Value, negative predictive Value of fecal Elastase 1 concentrations in different grades of chronic Pancreatitis

Chronic Pancreatitis °I-III n=201				
Cut off point	Sensitivity	Specificity	Pos pred value	Neg pred value
< 50 µg/g	18,4%	83,3%	94,9%	5,7%
<100 µg/g	29,9%	83,3%	96,8%	6,6%
< 200 µg/g	45,3%	75%	96,8%	7,6%
Chronic Pancreatitis °II-III n=148				
Cut off point	Sensitivity	Specificity	Pos pred value	Neg pred value
< 50 µg/g	24,3%	95,4%	92,3%	35,6%
< 100 µg/g	38,5%	92,2%	91,9%	39,7%
< 200 µg/g	57,4%	86,4%	90,4%	47,5%
Chronic Pancreatitis °III n=51				
Cut off point	Sensitivity	Specificity	Pos pred value	Neg pred value
< 50 µg/g	43%	89,5%	56,4%	83,3%
< 100 µg/g	52,9%	78,4%	43,5%	84,1%
< 200 µg/g	76,5%	66%	41,4%	82,9%

Figure 2: Frequency of normal and pathological fat excretion in 101 patients with fecal Elastase 1 concentrations < 100 µg/g

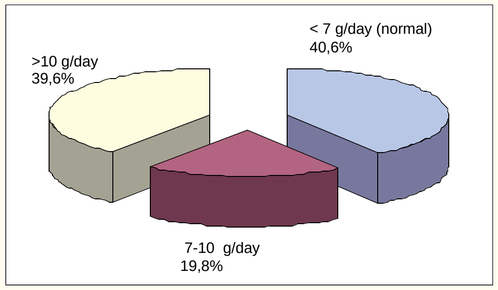

Table 3: Clinical findings in patients with fecal Elastase 1 concentrations < 100 µg/g

	1	2	3	4
Stool frequency/ Day	76,9 %	20,2 %	1,9%	1%
Stool consistence*	64,4%	8,7%	26,9%	
Abdominal pain **	87,5%	10,6%	1,9%	
Bloating ***	42,3%	39,4%	16,4%	1,9%

*1 = formed/normal; 2 = hard; 3 = watery **1 = no; 2 = mild; 3 = moderate
***1 = no; 2 = mild; 3 = moderate; 4 = severe

Discussion

In the present study we compared fecal elastase 1 measurements as a parameter of exocrine pancreatic function to ERCP findings, the gold standard imaging procedure of the pancreas. As expected from studies comparing direct function tests with ERCP-images [6], we found moderate correlations in mild and moderate pancreatic duct changes, but a good sensitivity in grade III changes. More important, we found a good specificity, meaning that if FEC are low, the probability of pathological changes of the pancreatic duct is very high. In addition to this important impact on morphological pancreatic changes, we could show that FEC levels < 100 µg/g represent significant fat maldigestion in the majority of cases. The fact that there was no correlation between clinical symptoms and pathological fat excretion underlines the impression that clinical findings are rather uncharacteristic and occur late in the course of the disease.

In conclusion, reduced elastase 1 levels seem to represent severe pathological changes of both, exocrine morphology and function. According to our experience, the measurement of fecal elastase1 concentrations provides an excellent screening tool to characterize patients with exocrine pancreatic diseases.

References

1 Löser C, Möllgaard A, Fölsch UR. Faecal elastase 1: a novel, highly sensitive, and specific tubeless pancreatic function test. Gut 1996; 39: 580-586.

2 Stein J, Jung M, Sziegoleit A, Zeuzem S, Caspary WF, Lembcke B. Fecal immunoreactive elastase-1: Evaluation of a new tubeless pancreatic function test in comparison with other indirect and direct tests for exocrine pancreatic function Clin Chem 1996; 42: 222-226

3 Lankisch PG, Schmidt I, König H, et al. Faecal elastase 1: not helpful in diagnosing chronic pancreatitis associated with mild to moderate exocrine pancreatic insufficiency. Gut 1998; 42: 551-554.

4 Amann ST, Bishop M, Curington C, Toskes PP. Fecal elastase 1 is inaccurate in the diagnosis of chronic pancreatitis. Pancreas 1996; 13: 226-230.

5 Walkowiak J, Herzig KH. Fecal elastase-1 is decreased in villous atrophy regardless of the underlying disease. Eur J Clin Invest 2001; 31: 425-430

6 Lankisch PH, Seidensticker F, Otto J, Luebbers H, Mahlke R, Stoeckmann F, Foelsch U, Creutzfeld W. Secretin-pancreocymin test (SPT) and endoscopic retrograde cholangiopancreatography (ERCP): both are necessary for diagnosing or excluding chronic pancreatitis. Pancreas 1996; 12: 149-152.