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Original Article

Pancreatic Elastase-1 Quick Test for rapid assessment of pancreatic status in cystic fibrosis patients

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Abstract

Background: At present, fecal elastase-1 ELISA determination is the most sensitive and specific tubeless pancreatic function test available. However, the results are not available the same day in routine clinical practice. This prospective study aims at evaluating the sensitivity and specificity of the Elastase-1 Quick™ Test by comparing the results with the ELISA test.
Methods: The study was composed of three groups: the screening-diagnosed cystic fibrosis (CF) patients (n = 28), the screened, but non-CF subjects (n = 36) and non-screened CF patients (n = 62). Pancreatic status (normal vs abnormal) was evaluated using the Pancreas Elastase-1 Quick™ Test. Fecal elastase-1 concentration was determined with a commercially available ELISA kit, used as reference. The cut-off for abnormal results was set at <200 μg/g of stool.
Results: The Pancreatic Elastase-1 Quick Test™ showed the following sensitivities and specificities in the studied groups: 92.8% and 96.6% in all subjects, 90.5% and 100% in screening samples, and 92.8 and 90.5% in CF patients.
Conclusion: Pancreatic Elastase-1 Quick Test™ proves to be a rapid and reliable option to qualitatively evaluate pancreatic function for diagnostic purposes in a clinical setting of CF care.

Keywords: Exocrine pancreatic insufficiency; Specificity; Sensitivity; Qualitative test; Point-of-care

1. Introduction

Cystic fibrosis (CF) is a disorder caused by mutations in the CF transmembrane conductance regulator (*CFTR*) gene. As a result, the increased viscosity of mucus blocks the ducts of exocrine glands such as the lungs and pancreas. In the latter case, this leads to severe exocrine pancreatic insufficiency with maldigestion in about 85–90% of CF patients, called pancreatic insufficient (PI). Nevertheless, patients evaluated as being pancreatic sufficient (PS) do not present steatorrhea, but may demonstrate decreased pancreatic volume, abnormal bicarbonate concentration and altered enzyme secretion due to the fact that fat malabsorption may not appear until there is a 98% loss of pancreatic function [1]. PI is the cause of malnutrition, poor clinical status and survival, so it is crucial to rapidly and accurately determine pancreatic status in CF patients.

The diagnosis can be obtained by direct and indirect testing. Direct tests for estimation of pancreatic function such as the gold standard secretin-cholecystokinin test are unsuitable (time consuming, invasive, and expensive) for routine evaluation in children. Therefore several indirect tests, including fecal chymotrypsin, pancreolauryl test, mixed triglyceride breath test and fecal elastase-1 assessment, have been developed and

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evaluated for diagnosing pancreatic status [2]. Human pancreatic elastase-1 is an endoprotease and sterol binding protein that remains stable through the intestinal passage. Its concentrations in feces reach up to 5–6 times higher than in pancreatic juice, which indicates that it can serve as a diagnostic tool for evaluating exocrine pancreatic function. To date, the test has been shown to have the highest sensitivity among indirect tests [3,4], especially in patients with severe exocrine pancreatic insufficiency [5–9].

Early delineation of PI subjects is crucial from a practical point of view. Moreover, the choice of the test should base on its sensitivity, specificity and noninvasiveness. Towards the need for rapid diagnosis of CF patients with pancreatic involvement, a novel test has been developed. This prospective study aims at evaluating the sensitivity and specificity of the Elastase-1 Quick Test by comparing the results with the ELISA test, the gold standard for non-invasive exocrine pancreatic function.

2. Methods

2.1. Subjects

The study was composed of three groups: the CF screened (28 subjects with CF aged from 1.5 to 3 months diagnosed in CF screening program), non-CF screened (36 subjects aged from 1.5 to 6.5 months in whom CF in the course of CF screening program was excluded) and CF non-screened (62 subjects diagnosed with CF in a classical way aged from 8 months to 25 years old) for a total of 126 subjects (53 females and 73 males) (Table 1). Participants were recruited at the Department of Pediatric Gastroenterology and Metabolic Diseases, Poznan, Poland and the Lviv Cystic Fibrosis Centre, Lviv, Ukraine. The diagnosis of CF was based on history, clinical manifestation, increased sweat chloride concentrations, and *CFTR* gene examination. The genotypes of the CF patients were as follows: F508del/F508del (n = 30), F508del/2184insA (n = 11), F508del/unknown mutation (n = 8), F508del/N1303 K (n = 5), F508del/1898 + 1G-A (n = 4), F508del/2143delT (n = 4), F508del/G542X (n = 4), F508del/dele2,3(21 kb) (n = 3), F508del/3849 + 10kbC/T (n = 2), F508del/3272-26A > G (n = 2), F508del/2721del11 (n = 1), E585X/1524 + 1G > A (n = 1), F508del/R553X (n = 1), C524X/G542X (n = 1), F508del/L88IfsX22 (n = 1), F508del/185 + 1G > T (n = 1), F508del/R347H (n = 1), N1303K/2183AA-G (n = 1), F508del/W1282X (n = 1), 2183AA > G/E92K (n = 1), 3849 + 10kbC > T/F1074L (n = 1), F508del/G85E (n = 1), F508del/621-1G > T (n = 1), 621-1G > T/3849 + 10kbC > T (n = 1), F508del/V1001-I1005del (n = 1), D806G/unknown (n = 1), L257G/unknown (n = 1). An informed written consent from the parents of each patient was obtained.

Table 1
Basic demographic data of the study subjects (n = 126).

			Age*		
Subjects			Mean	Median	1st–3rd quartile
Screening	CF (n = 28)	Total	2.3	2.0	1.9–2.3
		♀	2.2	2.0	1.5–2.0
		♂	2.4	2.0	2.0–3.0
	Non-CF (n = 36)	Total	2.9	2.5	2.0–3.5
		♀	3.0	2.5	1.8–3.8
		♂	2.8	2.5	2.0–3.5
Non-screening	CF (n = 62)	Total	9.0	8.0	4.8–12.5
		♀	8.3	7.4	4.6–10.9
		♂	9.5	8.6	5.0–13.9

* Months for screening, years in non-screening patients.

2.2. Protocol

Two small samples of feces were collected from the same stool sample of each subject. Fecal elastase-1 concentration was determined with a commercially available ELISA kit (ScheBo® Biotech AG, Giessen, Germany) [3,4]. The values of elastase-1 were rounded to the nearest integer and the cut-off value for abnormal results of the test was set at <200 μg/g in the stool. Evaluation of the pancreatic status was also done with the use of the Pancreas Elastase-1 Quick™ Test (ScheBo® Biotech AG, Giessen, Germany). The qualitative results of the test would present as two stripes for a positive (normal) result and one stripe for a negative (abnormal) result. The commercially available kits were kindly provided by ScheBo® Biotech AG.

The ScheBo Pancreas Elastase-1 Quick stool test is a visual immunochromatographic rapid test for the detection of pancreatic elastase-1 in stool samples. It is based on the same monoclonal antibodies as the Pancreatic Elastase-1 ELISA stool test. Elastase-1 in the stool sample reacts with a monoclonal antibody bound to gold particles. This complex migrates along the test membrane and reaches the test line (T) which has a second monoclonal antibody against elastase-1 attached. If the exocrine pancreatic function is normal (=high elastase-1 concentration) the gold labeled antibody + pancreatic elastase-1 complex binds to the test line (T) and a pink color develops. In the event of an exocrine pancreatic insufficiency (=low elastase 1 concentration) the sample does not contain antibody + elastase-1 complex that can bind to the test band (T) so no color becomes visible. Development of a pink control line (C) guarantees that sample application and migration have taken place correctly and that the test was properly performed. The appearance of two lines corresponds with fecal elastase-1 concentration >200 μg/g.

Table 2
Fecal elastase-1 concentrations (ELISA) in patients with normal and abnormal results of Elastase-1 Quick Test.

		Elastase-1 Quick Test	Elastase-1 [μg/g of stool]		
Subjects			Mean	Median	1st–3rd quartile
Screening	CF	Abnormal results	16	5	1–25
		Normal results	404	330	234–392
	Non-CF	Normal results	1129	1080	871–1332
Non-screening	CF	Abnormal results	26	1	0–4
		Normal results	847	963	270–1300