Synopsis of the publications concerning the Pancreatic Elastase ELISA from BIOSERV Diagnostics

Evaluation of a fecal pancreatic elastase-1 enzyme-linked immunosorbent assay: Assessment versus an established assay and implication in classifying pancreatic function

J A Erickson1, W E Aldeen2, D G Grenache1,3, E R Ashwood1,3, Published in: Clinica Chimica Acta, Volume 397, Issues 1-2, November 2008, Pages 87-91

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Background: Disagreement continues regarding 2 fecal pancreatic elastase-1 (PE-1) ELISAs and their respective capabilities to assess pancreatic function.

Methods: The Bioserv Diagnostics polyclonal PE-1 ELISA was validated and its performance characteristics compared to the previously validated ScheBo Biotech monoclonal PE-1 ELISA. Split sample study results were analyzed by Deming regression and Bland-Altman plot analysis. Data mining was utilized to explore PE-1 distribution and evaluate PE-1 and fecal fat correlation.

Results: Analysis demonstrates limited quantitative agreement; slope = 0.9640, intercept = 10.787, R² = 0.633. Means were 228.8 and 226.2 µg PE-1/g stool for the polyclonal and monoclonal assays respectively. Bland-Altman analysis showed 91 % of paired values within 2 SD of their means. There was good qualitative agreement when interpreted against established intervals with 91 % of results equivalent in pancreatic function classification. The remaining 9 % varied by one classification level with no bias evident. The distribution of PE-1 concentrations (n = 400, 0-25 years) classified 78 % of subjects with normal pancreatic function, 7 % with moderate pancreatic insufficiency and 15 % with severe insufficiency. There was little agreement between PE-1 and fecal fat results.

Conclusions: The polyclonal PE-1 ELISA is an acceptable alternative to the monoclonal PE-1 ELISA. PE-1 is a potential substitute for fecal fat for evaluating pancreatic function.

Specificity of the Polyclonal Antibody Test System For Human Elastase in Stool

C M Qualia1, J F Villalona1, C Ren2, T M Rossi1, Published in: Journal of Pediatric Gastroenterology and Nutrition, Vol. 45:E26 #66, No. 4 October 2007

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Background: Elastase is a proteolitic enzyme secreted by exocrine pancreatic tissue. Fecal elastase (FE) concentration has been shown to be a reliable indicator of exocrine pancreatic secretion. FE levels greater than 200µg/g of stool are consistent with pancreatic insufficiency. Both monoclonal and polyclonal antibody test systems for the detection of FE exist. While the monoclonal antibody test system utilizes a single antibody that binds to a specific epitope of human pancreatic elastase, the polyclonal system utilizes four different antibodies that bind to a synthetic peptide sequence contained
within human pancreatic elastase. The purpose of this study was to determine whether the antibodies employed by the polyclonal test system cross-react with porcine elastase contained in supplemental pancreatic enzymes.

**Methods:** Children age 0-18 years taking supplemental pancreatic enzymes were eligible for enrollment. Stool samples were collected from all patients while they were ingesting supplemental pancreatic enzymes. A proportion of patients then discontinued their supplemental enzymes for four days and a second stool sample was collected. All stool samples were tested by the polyclonal antibody test system (Bioserv, Rostock, Germany) for FE concentration.

**Results:** A total of 21 children were enrolled in the study. Eleven patients submitted stool samples both on and off enzymes, while ten patients submitted a single stool sample on enzymes. For all samples collected, the FE concentration was less than 200 µg/g of stool. The FE levels of stool samples obtained while patients were taking supplemental enzymes did not differ significantly from those collected off enzymes.

**Conclusion:** The polyclonal antibody test system for human elastase in stool does not detect porcine extracts present in exogenous pancreatic enzymes. This test system can be used to accurately determine the exocrine pancreatic function of children taking supplemental pancreatic enzymes.

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**Assessment of Isoform specificity of a polyclonal Elastase ELISA**

F U Weiss1, M Ruthenbürger1, E Hammer2, U Völker2, M M Lerch1. Published in: Journal of Pediatric Gastroenterology and Nutrition 43:E32 # 58, 2006

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**Introduction:** Elastase is secreted from the pancreas and passes through the GI-tract without significant degradation. Exocrine pancreatic function analysis can therefore be performed with Elastase stool tests. Five different isoforms of human pancreatic elastase (PA I, IIA, IIB, IIIA, IIIB) have been identified. Three different polyclonal antisera that are used in a commercial ELISA were investigated for their specific recognition of human elastase isoforms in human pancreatic juice.

**Material and Methods:** Secreted proteins from human pancreatic juice were analysed by one or two-dimensional gel-electrophoresis, followed by westernblot analysis using 3 different polyclonal anti-Elastase antibodies (BIOSERV GmbH, Germany) and MALDI-TOF-MS. Elastase-activity was analysed in immunoprecipitates from human pancreatic juice using a fluorogenic Elastase substrate. Finally, cross-reactivity of the antibodies was tested against pancreatin from pig pancreas.

**Results:** In 1D Western blots of pancreatic juice all three polyclonal antisera against human Elastase detected a single ~30kDa protein. Immunoprecipitates with these antibodies exhibited elastase activity as determined with the fluorogenic Elastase substrate. In 2D-Westernblots (pH3-10) proteins in the molecular weight range of ~30 kDa were separated into a number of spots of different isoelectric points (pl). MALDI-TOF-MS-Analysis of these spots revealed the presence of pancreatic Elastase IIIA and IIIB isoforms, but not Elastase II or Elastase I isoforms. Western blot analysis of pancreatin from pig pancreas revealed no cross-reactivity with any of the three antisera tested.
Conclusion: All three commercial antibodies that are used in a polyclonal Elastase ELISA preferentially detect human Elastase Isoforms IIA and IIIB, and do not cross-react with pig pancreatin. At present differences concerning expression and specific function of PA II or PA III isoforms are still unknown, but we could demonstrate, that PA III isoforms clearly possess Elastase activity as determined by a fluorogenic Elastase substrate. Elastase I ia not an enzyme expressed in the adult human pancreas and should therefore not be referred to in commercial test kits for exocrine pancreatic function.

Faecal elastase-1 concentration in cystic fibrosis patients with CFTR I1234V mutation

H. Abdel Rahman, A. Abdul Wahab, M.O. Abdel Rahman & Ossama Abdel Rahman Mostafa

Published in: Acta Paediatrica, 2006; 95: 1066-1069

Abstract

Aim: To assess the exocrine pancreatic function among cystic fibrosis patients with cystic fibrosis trans-membrane conductance regulator (CFTR) I1234V mutation. Methods: Cross-sectional study of 40 cystic fibrosis patients with homozygous CFTR I1234V mutation belonging to a large Arab kindred family and 25 healthy subjects as a control group over a period of 12 mo. Assessment of their exocrine pancreatic function was performed by measuring faecal elastase-1 (FE1) concentration with a commercial ELISA kit using polyclonal antibodies (BIOSERV Diagnostics) in CF patients compared to healthy subjects. The results were compared with those obtained from a second laboratory using another commercial ELISA (ScheBo; Biotech, Germany) that uses two monoclonal antibodies against different specific epitopes of human pancreatic elastase. Results: All CF patients with CFTR I1234V mutation had normal levels of faecal elastase 1. No significant difference was found between the two methods for the CF groups or between the CF patients with and without pancreatic enzyme replacement.

Conclusion: Cystic fibrosis with homozygous CFTR I1234V mutation is associated with pancreatic sufficiency. Assessment of exocrine function using polyclonal antibodies does not significantly differ from that using two monoclonal antibodies against different specific epitopes of human pancreatic elastase.

A New Fecal Elastase 1 Test Using Polyclonal Antibodies for the Detection of Exocrine Pancreatic Insufficiency

Jan-Uwe Hahn, Sabine Bochnig, Wolfgang Kerner, Helma Koenig, Birgit Sporleder, Paul Georg Lankisch, Patrick Maisonneuve, Albert B Lowenfels


Summary: The fecal elastase 1 test from BIOSERV Diagnostics was compared with the test of the competition, with the secretin-cerulein test as direct pancreatic function test (gold standard) and with the quantitative fecal fat analysis. 31 patients sent to the Department of Medicine at the Municipal Hospital in Lueneburg with suspected chronic pancreatitis were investigated. Exocrine pancreatic insufficiency was classified as mild, moderate or severe.
According to the results of the SCT, 11 of the 31 patients had exocrine pancreatic insufficiency that was due to chronic pancreatitis.

The sensitivity in detecting exocrine pancreatic insufficiency was 64% for both test procedures. The specificity of the new test was much higher than that of the older one (95% vs. 80%). When patients with severe exocrine pancreatic insufficiency were evaluated, the sensitivity of both tests was 83% and thus similar to those rates shown in previous studies for the monoclonal test.

Conclusion: .. the polyclonal test seems to have the same sensitivity as the monoclonal test but offers a higher specificity. Therefore, it is more useful for differentiating between pancreatic and nonpancreatic steatorrhea, which is a frequent clinical problem.

Polyclonal versus Monoclonal ELISA for the Determination of Fecal Elastase 1: Diagnostic Value in Cystic Fibrosis and Chronic Pancreatic Insufficiency.

Yvette Miendje, Diane Maisin, Marie J. Sipewa, Pierre Deprez, Jean P. Buts., Philippe De Nayer, Marianne Philippe

Published in: Clinical Laboratory, Vol. 50, No. 7+8, 2004; pp. 419 - 424

Summary: The authors collected single spot samples from two groups of patients. The group of adults included 13 healthy subjects (HS), 12 patients with non-pancreatic gastrointestinal disease (NPGD), 26 with chronic pancreatitis with presence of calcification (CCP) and 14 without calcification (NCP). The group of children included 17 cases of cystic fibrosis (CF) and 21 controls (CO). After a common extraction, both assays were performed as recommended by the manufacturers.

In the children group, Sensitivity was 94% for both assays. Specificity was 100% for the BIOSERV kit and 95% for the Schebo kit. For the adult group, Sensitivity was 82% for the BIOSERV kit and 80% for the Schebo kit. The specificity was 92% for both assays.

The interassay CVs computed from 12 consecutive assays of three different fecal samples (low, medium and high value) were 2.7 to 5.1% (mean 3.6%) and 3.7 to 5.9% (mean 5%) for Bioserv and ScheBo, respectively.

Both the kit from BIOSERV Diagnostics and the Schebo kit were found suitable for the detection of severe pancreatic insufficiency either in adult patients or in children. However, the specificity and the reproducibility of the BIOSERV Diagnostics kit was slightly better.

Clinical Value of a New Fecal Elastase Test for Detection of Chronic Pancreatitis

Volker Keim, Niels Teich, and Joachim Moessner

Published in: Clinical Laboratory, Vol. 49, No. 5+6, 2003; pp. 209 – 215

Summary: Fecal samples from 212 patients were taken. Chronic pancreatitis was assumed when ductal alterations were present in ERCP. The severity of disease was assessed according to the Cambridge classification. Elastase (test from ScheBo, Germany) and chymotrypsin (Roche Diagnostics) were measured. As a new parameter an Elastase ELISA from BIOSERV (Rostock, Germany) was employed. Specificity, sensitivity, and accuracy of each test as well as the ROC curves were calculated.

In 45 patients (21.2%) chronic pancreatitis was diagnosed.
Value of polyclonal Elastase ELISA for diagnosis of chronic pancreatitis

V. Keim. N. Teich, and J. Mössner.


Summary: BIOSERV superior to Schebo and to Chymotrypsin: Bioserv diagnostic specificity 12% better than Schebotech, accuracy 10% better, diagnostic sensitivity 2% better “... the newly available polyclonal pancreatic elastase assay was superior both to the monoclonal Elisa and to chymotrypsin.”

<table>
<thead>
<tr>
<th></th>
<th>Fecal Elastase 1 (BIOSERV)</th>
<th>Fecal Elastase 1 (ScheboTech)</th>
<th>Cymotrypsin (Roche Diagnostics)</th>
<th>Patient Types</th>
</tr>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>50%</td>
<td>48%</td>
<td>44%</td>
<td>64 patients diagnosed with chronic pancreatitis</td>
</tr>
<tr>
<td>Specificity</td>
<td>75%</td>
<td>63%</td>
<td>55%</td>
<td>out of 699 abdominal diseases</td>
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<tr>
<td>Accuracy</td>
<td>72%</td>
<td>62%</td>
<td>54%</td>
<td></td>
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<tr>
<td>Specificity</td>
<td>92%</td>
<td>86%</td>
<td></td>
<td>Healthy individuals (n=40) and blood donors (n=78)</td>
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Quantification of fecal Elastase-1 using either polyclonal or monoclonal antibodies.

Carlos A Garcia-Bueno, Thomas M (Michael) Rossi, Kusuma W Lee, Melawati T Yuwono, Mary Bridge, Amy Robinson, Amin Tjota

Abstract published in: Gastroenterology, vol 122, no 4 page A-510, April, 2002; Poster T1713 “The polyclonal antibody based method for detection of fecal E-1 is as sensitive as the monoclonal test system.”

Summary: Comparison of BIOSERV and Schebo to the secretin-pancreozymin test (gold standard).
BIOSERV at least as good as Schebo, both comparably to the gold standard.

Pierre H. Deprez, Milena Del Natale, Yvette V. Mienjje Deji, Stanislas Pauwels, Marianne Philippe


Summary: BIOSERV and Schebo better than Breath test. BIOSERV Diagnostics and Schebotech comparable, both better than Breath Test “The two FE tests were shown to be more suitable to diagnose exocrine pancreatic insufficiency than MT”.

Polyclonal versus monoclonal ELISA for the determination of faecal Elastase-1: Diagnostic Value in Cystic Fibrosis and Chronic Pancreatic Insufficiency

Yvette Mienjje Deyi, Pierre Deprez, Jean P. Buts, Diane Maisin, Marie J Sipewa, Philippe De Nayer and Marianne Philippe

Poster C25 at the 24th Annual Symposium of the BVKB-SBBC/BVKC-SBCC


Also available: Original poster (scan, pdf file, colour or black and white)

Summary: BIOSERV and Schebo kit suitable ... Comparison of the BIOSERV ELISA to the Schebo ELISA. “Both kits are suitable for the detection of severe insufficiency of pancreas either in adult patients or in children.”

Proper interpretation of Elastase-1 activities in Stool: experience of the Prague CF centre

Helena Tomášová, Dana Zemková, J. Bartosova, V. Skalicka, Stanislava Koloušková, Jirí Nevoral, Milan Macek Jr., Vera Vávrová

Poster 237 at the 25th Congress of the European Cystic Fibrosis Society, Genova, Italy, 20-23 June 2002

Published in:
  ○ (Abstract) Journal of Cystic Fibrosis, the Official Journal of the European Cystic Fibrosis Society, Volume 1, Supplement 1, page 138, ISSN 1569-1993

Also available: complete original poster (directly generated pdf)

Summary: Use of BIOSERV Elastase-1 ELISA in research and routine. Elastase-1 examination represents a noninvasive, relatively simple method, assessing the exocrine pancreatic function. In patients suffering from Cystic Fibrosis the exocrine pancreatic function is severely impaired, whereas the impairment in patients suffering from Diabetes mellitus type 1 seems to be less grave than in Cystic Fibrosis.
Experiences with fecal Elastase-1 determination in children with and without pancreatic insufficiency

Helena Tomášová, Vera Vávrová, Dana Zemková, Jiří Nevoral, Stanislava Koloušková, B Kočmichová, Milan Macek Jr.

Poster 112 at the Meeting of the Czech and Slovak Physiological Societies, Plzen, February 7th, 2003

Summary: Fecal elastase examination represents a non-invasive, simple method for assessing the exocrine pancreatic function. Whereas in 124 controls without pancreatic or intestinal disorders the secretion of E1 was normal, it was significantly decreased in IDDM patients and very much decreased in CF patients. Correlation with sweat Cl⁻ and with the CFTR genotype in CF patients was highly significant. E1 determination seems to be more sensitive than other indirect tests like chymotrypsin and does not require the interruption of an enzyme substitution therapy.

The Frequency of exocrine pancreatic insufficiency in Diabetes mellitus type 1 – also a methodical problem?

Hahn, J.-U., Wadowska, K., Heinke, P., Peters, H., Rjasanowski, I., Kerner, W.

Poster 20-04 at the 36th Annual Meeting of the German Diabetes Society

Published in: Diabetes und Stoffwechsel, 10, Suppl. 1 (2001)

Summary: Schebo finds many more ostensibly pancreatically insufficient patients than BIOSERV, probably due to the lack of diagnostic specificity of the Schebo assay. More soon to come.

Elastasi fecale e pancreatite cronica

Esposito C., Formicola V., Spanò A., Spina M.

Use of the BIOSERV Elastase-1 in the routine laboratory.

"Attualmente la determinazione dell'elastasi fecale con metodica Elisa è un presidio di prima scelta nella diagnostica dell'insufficienza escrinca del pancreas. E' un test di facile e rapida esecuzione per il laboratorista con il vantaggio di non essere invasivo per il paziente."