Faecal elastase 1 concentration is a marker of duodenal enteropathy

M G Schäppi, V V Smith, D Cubitt, P J Milla, K J Lindley

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Patients

Retrospective analysis was undertaken of all children between March 1997 and February 2000, who had undergone (1) small intestinal biopsy and (2) FE1 measurement within a month of each other at Great Ormond Street Hospital.

Faecal elastase 1

FE1 concentrations were measured using an enzyme linked immunosorbsent assay (ELISA) kit, which uses two monoclonal antibodies against two distinct epitopes of human pancreatic FE1 (Schebo Tech, GmbH, Wettenberg, Germany). The assay is linear between 15 and 400 µg elastase per g faecal weight with a lower detection limit of 15 µg/g. Results were expressed as µg/g of stool and nominally scored as indicative of normal pancreatic exocrine function (>200 µg/g), moderate pancreatic exocrine insufficiency (100–200 µg/g), or severe pancreatic exocrine insufficiency (<100 µg/g). Excessive stool water may be associated with falsely low faecal elastase concentrations and liquid stool samples were therefore discarded.

Secretin–cholecystokinin (CCK) test

In a small number of children, with a faecal elastase less than 200 µg/g, the secretin–CCK test, a direct test of pancreatic exocrine function, was performed. For this a tube was placed under fluoroscopy in the third part of the duodenum. Duodenal juice was aspirated over a 15 minute period and collected in plastic tubes on ice. Further samples were collected during consecutive 15 minute periods following injection of intravenous secretin (2 IU/kg), and subsequently intravenous CCK (2 µg/kg) and subsequently intravenous CCK (2IU/kg), which stimulates pancreatic ductal and acinar secretion respectively. Duodenal juice volume, pH, bicarbonate, lipase, and trypsin concentrations were determined in the laboratory.

Duodenal histology

Histological sections of duodenal mucosa stained with haematoxylin and cosin (H&E) were examined by light microscopy in a double blind fashion by an experienced paediatric histopathologist and a paediatric gastroenterologist. The morphology was assessed by measuring villus to crypt ratio (VCR) and scored in the following manner: 0 = flat mucosa, 1 = severe partial villous atrophy (PVA) (1:0 VCR), 2 = moderate PVA (1.5:1 VCR), 3 = mild PVA (2:2.5:1 VCR), 4 = normal VCR. Inflammation within the lamina propria of the biopsy specimens was scored (3 = no inflammation present, 2 = mild infiltrate of plasma cells, 1 = notable infiltrate).

Abbreviations: CCK, cholecystokinin; FE1, faecal elastase; GI, gastrointestinal; PI, pancreatic exocrine insufficiency; PZ, pancreozymin; PVA, partial villous atrophy; VCR, villus to crypt ratio.
Statistical analysis

Statistical analysis was performed using t test and regression analysis.

RESULTS

A total of 51 patients (24 boys, 27 girls; aged 27 days to 12 years) fulfilled the study entry criteria. FE1 was measured 60 times in 51 patients within a month of duodenal biopsy, nine patients having undergone both investigations a second time during a subsequent investigative episode. The intravenous secretin–CCK stimulation test had been undertaken in six of 51 patients during this same period.

The patients fell into nine diagnostic categories based on clinical and histopathological criteria: autoimmune enteropathy, indeterminate enteropathy, post-infectious enteropathy, tufting enteropathy, food sensitive enteropathy, food allergy without enteropathy, short gut syndrome with enteropathy, idiopathic inflammatory bowel disease (Crohn's disease), and failure to thrive without gastrointestinal (GI) cause. Figure 1 shows stool elastase concentrations for each of the diagnostic groups.

When mucosal morphology was compared with concentrations of FE1, using linear regression analysis, a highly significant correlation was shown between faecal elastase and duodenal morphology (t ratio 4.55; p < 0.0001; fig 2, table 1). Twenty six estimations were compatible with normal exocrine pancreatic function (>200 µg/g), 17 with moderate (100–200 µg/g), and 17 with severe (<100 µg/g) pancreatic insufficiency. Of the 26 normal results, 19 (73.1%) were matched with normal duodenal mucosal biopsy specimens and seven (26.9%) with enteropathies. Of the 17 (28.4%) stool elastase concentrations between 100 and 200 µg/g, six (35.3%) had normal histology and 11 (64.7%) enteropathies. Of the 17 (28.4%) stool elastase concentrations below 100 µg/g, only one (5.9%) had normal mucosa and 16 (94.1%) had enteropathies. In patients with normal small bowel morphometry and low FE1, we found inflammation to be present in 6/7 (85.7%), compared with 4/19 (21.1%) of patients with normal morphology and normal FE1. Table 1 summarises these results according to clinical diagnosis.

Inflammation was found to correlate with concentrations of FE1 (fig 3, table 2). Linear regression analysis showed the

Table 1 Comparison of faecal elastase 1 concentration with duodenal morphology

<table>
<thead>
<tr>
<th>Morphology</th>
<th>FE1 levels (µg/g)</th>
<th>&gt;200</th>
<th>100–200</th>
<th>&lt;100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal mucosa (score 4)</td>
<td>10 food allergy 2 post-infectious 4 FIT 2 AIE 1 IE</td>
<td>3 food allergy 1 AIE 1 FSE</td>
<td>1 post-infectious</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>19 (31.7%)</td>
<td>6 (10%)</td>
<td>1 (1.7%)</td>
<td></td>
</tr>
<tr>
<td>Mild PVA (score 3)</td>
<td>1 FSE 1 SGS</td>
<td>1 food allergy 1 SGS 1 AIE</td>
<td>1 FSE</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2 (3.3%)</td>
<td>3 (5%)</td>
<td>1 (1.7%)</td>
<td></td>
</tr>
<tr>
<td>Moderate PVA (score 2)</td>
<td>2 AIE 1 IE</td>
<td>1 FSE 1 AIE</td>
<td>2 FSE</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2 (3.3%)</td>
<td>1 (1.7%)</td>
<td>4 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Severe PVA (score 1)</td>
<td>1 AIE 1 FSE 2 SGS</td>
<td>1 tufting 2 IBD</td>
<td>4 AIE</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1 (1.7%)</td>
<td>3 (5%)</td>
<td>8 (13.3%)</td>
<td></td>
</tr>
<tr>
<td>Flat mucosa (score 0)</td>
<td>2 AIE 1 IE 1 tufting</td>
<td>2 AIE 1 FSE</td>
<td>1 tufting</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2 (3.3%)</td>
<td>4 (6.7%)</td>
<td>3 (5%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>26 (43.3%)</td>
<td>17 (28.4%)</td>
<td>17 (28.4%)</td>
<td></td>
</tr>
</tbody>
</table>
| Normal VCR (Morphology score) | 4 = normal VCR 3 = 2–2.5:1 VCR 2 = 1.5:1 VCR 1 = 1:1 VCR 0 = flat mucosa. PVA, partial villous atrophy; AIE, autoimmune enteropathy; FSE, food sensitive enteropathy; FIT, failure to thrive without GI cause; IBD, idiopathic inflammatory bowel disease; SGS, short gut syndrome; IE, indeterminate enteropathy; tufting, tufting enteropathy (epithelial dysplasia). 

Figure 2 Comparison of FE1 concentration with duodenal morphology. 4 = normal VCR, 3 = 2–2.5:1 VCR (mild PVA), 2 = 1.5:1 VCR (moderate PVA), 1 = 1:1 VCR (severe PVA), 0 = flat mucosa.
The exocrine pancreas secretes digestive enzymes (acinar tissue) and bicarbonate (ductal tissue). The secretory process is driven by neurohumoral events dependent on the presence of food within the duodenal lumen. Nutrient sensing is undertaken both by vagal afferent nerves and by mucosal enteroendocrine cells. Enteroendocrine cells secrete cholecystokinin in response to intraduodenal lipid/proteins, which stimulates pancreatic acinar secretion of zymogens.

DISCUSSION

The secretory process is best used to measure pancreatic exocrine function. Direct methods are labour intensive and invasive. They are best undertaken in centres in which there is a regular clinical need for the investigation so that staff and laboratory alike are competent in carrying out the investigation. Indirect methods include measurement of pancreatic digestive activity (PABA test, $^{13}$C triglyceride breath test$^{12}$) or measurement of pancreatic enzymes in the stool (faecal chymotrypsin and elastase). Most suffer shortcomings relating to the complexity of the test and/or poor sensitivity/specificity. In recent years faecal elastase determination has become a popular screening investigation for pancreatic exocrine insufficiency because it is simple, cheap, reliable, and widely available.

The assay is reported to have a high sensitivity and specificity in diagnosing severe primary pancreatic exocrine insufficiency$^{4, 13}$ (93–100% sensitivity, 83–100% specificity$^{15, 17, 19, 20}$) when

### Table 2

Comparison of faecal elastase concentration with duodenal inflammation

<table>
<thead>
<tr>
<th>Inflammation</th>
<th>FE1 levels (µg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;200</td>
</tr>
<tr>
<td>No inflammation</td>
<td>7 food allergy</td>
</tr>
<tr>
<td>(score 3)</td>
<td></td>
</tr>
<tr>
<td>4 FIT</td>
<td></td>
</tr>
<tr>
<td>2 AIE</td>
<td></td>
</tr>
<tr>
<td>2 post infectious</td>
<td></td>
</tr>
<tr>
<td>1 FSE</td>
<td></td>
</tr>
<tr>
<td>1 SGS</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>17 (28.3%)</td>
</tr>
<tr>
<td>Moderate infiltrate</td>
<td></td>
</tr>
<tr>
<td>(score 2)</td>
<td></td>
</tr>
<tr>
<td>3 food allergy</td>
<td></td>
</tr>
<tr>
<td>2 AIE</td>
<td></td>
</tr>
<tr>
<td>2 post infectious</td>
<td></td>
</tr>
<tr>
<td>1 FSE</td>
<td></td>
</tr>
<tr>
<td>1 SGS</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5 (8.3%)</td>
</tr>
<tr>
<td>Severe infiltrate</td>
<td></td>
</tr>
<tr>
<td>(score 1)</td>
<td></td>
</tr>
<tr>
<td>3 AIE</td>
<td></td>
</tr>
<tr>
<td>1 IE</td>
<td></td>
</tr>
<tr>
<td>1 post infectious</td>
<td></td>
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<td>4 (6.7%)</td>
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</tbody>
</table>

PVA, partial villous atrophy; AIE, autoimmune enteropathy; FSE, food sensitive enteropathy; FIT, failure to thrive without GI cause; IBD, idiopathic inflammatory bowel disease; SGS, short gut syndrome; IE, indeterminate enteropathy; tufting, tufting enteropathy (epithelial dysplasia).
values of <200 μg/g are used to indicate pancreatic insufficiency. Patients with small bowel mucosal damage, in association with coeliac disease, have also been found to have low FE1 concentrations,\(^7\) which increase to normality\(^7\) with the restoration of the mucosa integrity on a gluten free diet.\(^7\) Our study in children with reduced stool elastase and normal CCK–PZ tests provides evidence that the secretory capacity of the pancreas is normal in individuals with enteropathy. Thus the most likely mechanism of functional PI is a reduction in pancreatic stimulation with impaired secretion of secretin or CCK by the inflamed intestine.\(^7\) There remains a possibility of reduced pancreatic exocrine synthesis as a result of long standing malnutrition or primary pancreatic impairment.\(^8\) Low values of FE1\(^7\) and other pancreatic enzymes\(^7\) have been noted in other primary GI mucosal diseases and regarded as either false positive results\(^7\) or just been discarded.

This study clearly shows that small intestinal enteropathy of various origins is associated with reduced excretion of faecal elastase. The presence of inflammation within the duodenal mucosa has a profound negative effect on the exocrine pancreatic function. The link between mucosal inflammation and impaired pancreatic exocrine function impairment remains poorly understood, although it seems reasonable to propose that the enteroendocrine or neuroendocrine drive of the pancreas by the duodenum is perturbed in some way.

**Conclusion**

This study supports the notion that small bowel mucosal integrity is necessary for normal control of exocrine pancreatic secretion. It highlights the need for gastrointestinal mucosal biopsy in individuals with reduced FE1 concentrations in whom causes of primary pancreatic insufficiency (principally cystic fibrosis and Shwachman’s syndrome) have been excluded.

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**REFERENCES**


22 Lankisch PG, Schmidt I. Fecal elastase 1 is not the indirect pancreatic function test we have been waiting for. *Dig Dis Sci* 2000; 45: 166–7.

23 Amann ST, Taskes PP. Faecal elastase 1 [letter]. *Gut* 1997; 41: 419.

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