Faecal elastase 1 levels in premature and full term infants

M Kori, A Maayan-Metzger, R Shamir, L Sirota, G Dinari

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Background: Determination of faecal elastase 1 (FE1) is a simple, relatively inexpensive, non-invasive, highly specific and sensitive test for determining pancreatic function. Secretion of pancreatic enzymes varies during infancy, but there are almost no specific data on the ontogeny of elastase 1 in human babies. Aim: To study FE1 levels in preterm and term babies, and to determine the possible effect of gestational and postconceptual age on these levels.

Methods: Serial stool samples were collected and tested for FE1 level from 77 premature and full term infants. FE1 levels were determined by a commercially available enzyme linked immunosorbent assay (ELISA) kit.

Results: A total of 232 stool samples were collected from 77 neonates. The FE1 level measured in the first stool sample (meconium) was below normal (200 µg/g stool) in all samples regardless of gestational age. Sixty three neonates had at least two samples tested for FE1 level. The mean (SD) level of FE1 in sample 1 was 45.9 (51.1) µg/g stool and was significantly (p < 0.001) lower than in sample 2 (243.0 (164.9) µg/g stool). The lower the gestational age of the newborn, the more time it took for FE1 to reach normal levels.

Conclusions: FE1 levels in meconium are low, and studies in meconium should be avoided if pancreatic sufficiency is to be determined. FE1 reaches normal levels by day 3 in term newborns and by 2 weeks in infants born before 28 weeks gestation. Normal levels are reached sooner in infants of more advanced gestational age who start enteral feeding earlier.

Patients and methods

Serial stool samples were collected and tested for FE1 levels from 77 newborn infants (69 premature and eight full term infants) admitted to the neonatal intensive care unit and nursery at Schneider Children’s Medical Center of Israel.

The first stool sample was collected within the first 4 days of birth, and in most cases within 48 hours of birth. Two to four further stool samples were taken twice weekly. All stool samples were stored at −4°C to −8°C until analysis.

Data on gestational age, birth weight, sex, age, weight, and feeding status at each sampling were recorded.

FE1 level was determined with a commercially available enzyme linked immunosorbent assay (ELISA) kit (ScheBo-Tech, Wettenberg, Germany), which uses two monoclonal antibodies against specific epitopes of human pancreatic elastase. According to the manufacturer, FE1 concentrations of more than 200 µg/g stool indicate normal pancreatic function, levels of 100–200 µg/g stool indicate mild to moderate pancreatic insufficiency, and severe exocrine pancreatic insufficiency is indicated by levels below 100 µg/g stool. These reference levels only refer to adults.

Statistical analysis

The analysis was performed using BMDP statistical software. As the data for elastase did not distribute normally, we applied a square root transformation. We used the following statistical tests: Pearson’s χ² test, Pearson’s correlation, one way analysis of variance, and analysis of variance with repeated measures.

Results

A total of 232 stool samples were collected from 77 neonates. The mean (SD) gestational age of the study group was 30.9 (3) weeks (range 23–40). Mean (SD) birth weight was 1535 (701) g (range 490–4170). There were 48 male newborns and 29 female. Five newborns died during the study period. Enteral feeding was started at a mean (SD) age of 3.4 (3.1) days (range 1–13).
Faecal elastase 1 levels

Sixty three newborns had at least two samples of stool available for FE1 determination, the first sample of which was meconial, and taken before day 4 (most samples were collected by day 2). FE1 level measured in the first, meconial stool sample was below 200 µg/g in all samples regardless of gestational age. The mean (SD) level of FE1 in sample 1 was 49.5 (51.1) µg/g stool and was significantly (p < 0.001) lower than in sample 2 (243.0 (164.9) µg/g stool).

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>No</th>
<th>Sample 1</th>
<th>Sample 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;28</td>
<td>12</td>
<td>28.8 (39.6)</td>
<td>139.9 (127.2)</td>
</tr>
<tr>
<td>28–30</td>
<td>7</td>
<td>76.7 (70.5)</td>
<td>184.8 (113.4)</td>
</tr>
<tr>
<td>31–32</td>
<td>18</td>
<td>31.8 (31.5)</td>
<td>182.1 (128.6)</td>
</tr>
<tr>
<td>&gt;33</td>
<td>26</td>
<td>55.3 (57.2)</td>
<td>348.4 (160.5)</td>
</tr>
<tr>
<td>All</td>
<td>63</td>
<td>45.9 (51.1)</td>
<td>243.0 (164.9)</td>
</tr>
</tbody>
</table>

Results are expressed as mean (SD).

In the group of infants who eventually reached normal FE1 levels, 10 meconium samples were mixed with non-meconial stools in a 1:1 ratio. FE1 levels were determined before and after the mixture. The level of FE1 in the mixture was proportional to the level in the non-meconial stool sample, excluding a possible inhibitory effect of meconial factors (data not shown).

We examined the possible correlation between FE1 levels and gestational age, birth weight, and the age at which enteral feeding was started. There was a positive correlation between gestational age and FE1 level (r = 0.29, p < 0.01), and the level of FE1 was higher in newborns of more advanced gestational age.

In all full term newborns, the level of FE1 in sample 2 was normal. In the whole study group, there were 72 newborns in which FE1 eventually reached a normal level. We calculated the age at which the FE1 level reached normal values in the preterm infants with serial samples of FE1. Premature infants born at less than 28 weeks gestation reached normal FE1 at a mean of 12 days after birth, infants born at 28–32 weeks gestation at 8.4 days, infants born at 32–34 weeks gestation at 5.6 days, and infants born after 34 weeks gestation at 2.8 days. The lower the gestational age, the longer it took FE1 to reach normal levels (r = -0.55, p < 0.001). The same was true for birth weight (r = -0.45, p < 0.001).

In the group of infants who eventually reached normal FE1 levels, a strong negative correlation was found between gestational age and the first enteral feed (r = -0.65, p < 0.001). There was a positive correlation between the age at which enteral feeding was started and FE1 levels: the later enteral feeding was started, the lower FE1 reached normal levels (r = 0.5, p < 0.001).

DISCUSSION

Pancreatic elastase 1 is a specific human protease with elastolytic activity, synthesised by pancreatic acinar cells. Pancreatic elastase is not degraded during intestinal transit and is species specific. FE1 levels correlate well with direct tests of pancreatic function. Previous studies have shown that, at birth, protease levels are close to adult levels, but there are only a few studies of the specific human protease, elastase 1, in preterm and term newborns. Nissler et al measured pancreatic elastase 1 concentration in faeces of 148 infants up to 12 months of age. They found that over 96% of infants had elastase 1 concentrations greater than an adult lower limit of normal after 2 weeks of life, independent of gestational age and the type of nutrition. Up to 48 hours after birth, 43% of term infants had normal adult values, whereas none of the preterm infants had elastase 1 concentrations in the normal range.

Von Seebach & Henker measured FE1 levels in 28 preterm and 27 term newborns. The mean level of FE1 in meconium was 63.9 µg/g stool and rose to over 200 µg/g at 1 month of age, independently of gestational age. In another study, FE1 levels rose to normal by 2 weeks.

The aim of our study was to measure FE1 levels in preterm and term babies, and to determine the possible effect of gestational and postconceptual age on these levels and pancreatic function. Our results show that the level of FE1 in meconium is low, compared with the level in stool taken at a later age, regardless of gestational age. The chronological age at which the level of FE1 was determined had major importance. FE1 levels determined during the first days of life in meconium samples were significantly lower than levels determined later. In full term newborns the second sample taken by day 3–4 was normal. In premature infants, the lower the gestational age of the infant, the longer it took FE1 to reach normal levels, but even in the very premature infants, born at 28 weeks gestation or less, FE1 reached normal levels by 2 weeks of age. The results of mixing meconium and regular stools excluded the possibility of an inhibitory factor in the meconium.

We also showed that the earlier the newborn starts feeding, the sooner FE1 reaches normal levels. This may be related to earlier elastase secretion with feeding or may possibly be due to relative pancreatic insufficiency in very premature sick infants not being fed.

In conclusion, FE1 levels in meconium are low and do not indicate pancreatic insufficiency. FE1 reaches normal levels by day 3–4 in term newborns and by 2 weeks of age in infants born before 28 weeks gestation. FE1 reaches normal levels sooner in infants of more advanced gestational age who start enteral feeding earlier.

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Authors’ affiliations

M Kori, R Shamir, G Dinari, Institute of Pediatric Gastroenterology and Nutrition, Schneider Children’s Medical Center of Israel, Petah Tikva, Israel
A Maayan-Metzger, L Sirota, Neonatal Intensive Care Unit, Schneider Children’s Medical Center of Israel

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