SHORT REPORT

Low levels of pancreatic elastase 1 in stools of preterm infants

F Campeotto, N Kapel, N Kalach, H Razafimahefa, F Castela, L Barbot, P Soulaines, M Dehan, J G Gobert, C Dupont

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The amount of faecal pancreatic enzyme elastase 1 was significantly lower in 42 preterm newborns than in 12 full term babies at day 2 (89 (3–539) *v* 354 (52–600) µg/g, p<0.0007) and day 5 (164 (3–600) *v* 600 (158–600) µg/g, p<0.05) and correlated positively with total nutrient intake during the first week of life in preterm infants. This should probably be taken into account during early feeding.

Pancreatic elastase 1 (E1) is considered to be a highly sensitive and specific marker for exocrine pancreatic function, allowing the diagnosis of pancreatic insufficiency at all ages.[1] After two weeks of life, whatever the gestational age, 96.8% of infants without pancreatic disorders exhibit faecal E1 levels comparable to those of adults.[2] A preliminary study suggested decreased faecal E1 levels in infants below 2 weeks of age,[3] and this prospective study measured faecal E1 in preterm and full term newborn infants during the first week of life.

METHODS AND RESULTS

A bicentric prospective study enrolled 42 preterm infants (18 girls and 24 boys) born at 28 weeks gestation (median, range 25–35 weeks) and weighing 1140 g (range 640–1890), including 13 extreme premature infants (< 28 weeks gestation). Controls were 12 full term infants (eight girls and four boys) born at term (38–41 weeks) and weighing 3455 g (range 2840–4160).

For each child, one to three stool samples (about 5 g) were obtained during the first two weeks of life and stored at −20°C before analysis. The first sample was obtained between days 0 and 7 (median 2), the second between days 3 and 9 (median 5), and the third between days 7 and 11 (median 9). Owing to monitoring difficulties, two stool samples were collected for 29 of the 42 premature infants and three for the remaining 12. Three stool samples were not collected for any of the term infants, as they were discharged at 5 days of age.

Pancreatic E1 levels were determined using a "sandwich" type enzyme immunoassay (Schebo-Biotech, Guiessen, Germany), using two monoclonal antibodies binding to two distinct epitopes specific to human pancreatic E1. Results were expressed as µg/g of stool; 200 µg/g was the lower normal limit.[1] All quantitative results are given as median (range).

Statistical comparisons were performed using the non-parametric Mann-Whitney U test. Single regression analysis was used to calculate correlation coefficients for parametric data.

In all newborns, faecal E1 levels increased significantly (p<0.0001) from the first to the third sample: 113 (3–600), 242 (3–600), and 459 (559–600) µg/g respectively. E1 levels were significantly lower in preterm infants than in full term infants at day 2 (89 (3–539) *v* 354 (52–600) µg/g, p<0.0007) and day 5 (164 (3–600) *v* 600 (158–600) µg/g, p<0.05) (fig 1). No difference was found between extremely premature (74 (3–228) µg/g) and premature infants (102 (3–539) µg/g) (p = 0.58), within the first week of life. All preterm infants displayed normal E1 levels from the second week onwards.

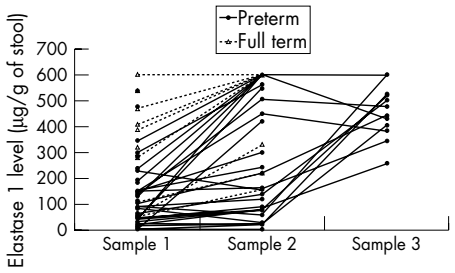

Figure 1 Pancreatic elastase (E1) levels in the two groups of newborn infants. Samples 1, 2, and 3 were collected on median day 2, median day 5, and median day 9 respectively. Reference concentrations for pancreatic E1 in adult stools are: normal, ⩾ 200 µg/g; moderate to light exocrine pancreatic insufficiency, 100 to < 200 µg/g; severe pancreatic insufficiency, ⩽ 100 µg/g.

Considering all infants, a positive correlation was observed between E1 levels and gestational age in both first week samples: $r = 0.5$, p = 0.0001 and $r = 0.3$, p = 0.03. A positive correlation was also observed between E1 levels in the first sample and birth weight: $r = 0.5$, p = 0.0001.

In preterms, a positive correlation was observed between E1 levels in the first sample and total energy ($r = 0.47$, p = 0.002), lipid ($r = 0.43$, p = 0.004), protein ($r = 0.45$, p = 0.002), and carbohydrate ($r = 0.47$, p = 0.001) intake (fig 2).

No correlation was found between faecal E1 and any of the other clinical parameters of the studied population: sex, maternal treatment with steroids, maternal blood hypertension, acute fetal distress, infection, respiratory distress, intrauterine growth retardation, necrotising enterocolitis, treatment, the day of stool sampling (table 1).

DISCUSSION

Preterm infants have low levels of faecal E1 during the first week of life, whereas full term infants do not, suggesting exocrine pancreatic immaturity in the former. The beneficial effect of early enteral feeding on pancreatic exocrine function is supported by the correlation between faecal E1 increase and nutrient intake.

Considerable variations in faecal E1 between stool samples and from day to day have been described by Hamwi *et al*.[4] The first sample was obtained close to birth, according to the availability of stools during this period of intensive care. This collection may have involved either stool or meconium, which is known to contain low E1 levels.[2 5]

More than half (52%) of preterm infants still had low pancreatic E1 (< 200 µg/g of stool) at the end of the first week,

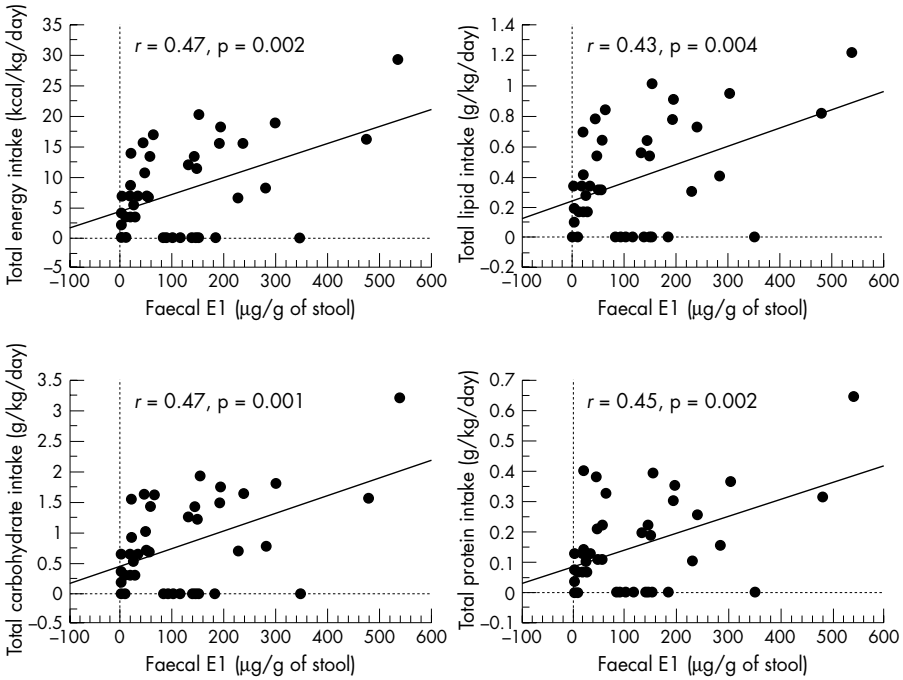

Figure 2 Correlation between faecal elastase 1 (E1) level and nutritional intake in preterm infants in the first sample.

Table 1 Clinical features of the 42 preterm infants

	Preterm infants
Sex (F:M)	18:24
Gestational age (weeks)	28 (25–35)*
Birth weight (g)	1140 (640–1890)*
Maternal steroids	33 (78%)
Maternal hypertension	11 (26%)
Acute fetal distress	12 (28%)
Infection	8 (19%)
Respiratory distress	39 (93%)
Intrauterine growth retardation	7 (17%)
Necrotising enterocolitis	1 (2.4%)
Steroids	17 (40%)
Sedation	24 (57%)
Inotropes	5 (12%)
Volume expansion	9 (21%)
Insulin	2 (5%)
Feeding	29 (70%)

*Values are median (range).

independent of gestational age. Maturation occurs in preterm infants as well as in full term babies after the first week of life, as described by Terbrack *et al*[5] and Von Seebach and Henker[2]: after one week of life, 97.4% of term infants (but only 85% of preterm babies) had reached adult levels of E1 of > 200 µg/g faeces. After the first week of life, E1 concentrations remained within the normal adult range. The levels observed during the first week of life remained above values currently observed in cystic fibrosis (< 50 µg/g of stool).[6]

The positive correlation between energy and nutrient intakes during the first week of life in preterm infants supports "minimal enteral feeding" as a strategy for accelerating the maturation of gastrointestinal function.[7] Digestion of nutrients in preterm infants may not be optimal in the first week of life, despite increased needs. Therefore, the trend to sustain "early aggressive enteral feeding"[8] has probably to be dealt with taking into account pancreatic immaturity: an adaptation of nutrients during the first week seems desirable.

Conclusion

A pancreatic maturation deficit exists in the first week of life in preterm infants, depending on gestational age. E1 levels normalise within the first days, more rapidly with enteral nutrition. This should be taken into account during early feeding of preterm infants.

Authors' affiliations

F Campeotto, N Kalach, F Castela, P Soulaines, C Dupont, Service de Néonatologie, Hôpital Cochin-Saint Vincent de Paul, 82 Avenue Denfert Rochereau, 75674 Paris Cedex 14, France and Université René Descartes, Paris V, France

N Kapel, L Barbot, J G Gobert, Service de Coprologie Fonctionnelle, Groupe Hospitalier Pitié-Salpetrière, 47 Boulevard de l'Hôpital, 75651 Paris Cedex 13, France

H Razafimahefa, M Dehan, Service de Réanimation Néonatale, Hôpital Antoine Béclère, 157 rue de la Porte-de-Trivaux, 92141 Clamart, France

Correspondence to: Dr Campeotto, Service de Néonatologie, Hôpital Saint Vincent de Paul, 82 Avenue Denfert Rochereau, 75674 Paris cedex 14, France; florence.campeotto@noos.fr

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