Neonatal gut function, measured by the one hour blood D (+) xylose test: influence of gestational age and size

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SUMMARY D(+) Xylose absorption, assessed by one hour blood xylose levels, has been measured after intraduodenal infusion of the sugar in 35 infants of differing gestational age and size. The test was performed between the 2nd and 6th days of life. Full-term appropriately grown infants had higher blood xylose levels (1.41 ± 0.07 mmol/l) at one hour than pre-term appropriately grown infants (1.17 ± 0.07 mmol/l; $P < 0.05$), or 'light for dates' infants, both full-term (0.73 ± 0.06 mmol/l; $P < 0.001$) and pre-term (0.96 ± 0.17 mmol/l; $P < 0.05$). Serial studies of 11 infants were made two to five times between the 3rd and 20th day of life. The levels for one hour xylose rose in all groups, but the 'light for dates' infants showed the least rise. There was no sign of catch-up in this group, and some results appeared to fall further behind those of appropriately grown infants. These results suggest that the primal small intestine is maturing in the perinatal period, and that intrauterine growth retardation may impair intestinal absorption. The nutritional significance is not known.

Optimal nutritional intake for low birthweight infants is believed to be important for the quality of long-term growth and development¹, yet the intestinal absorptive capacity of these infants has been little studied.

The human foetal small intestine is changing rapidly in the last trimester of pregnancy. *In vitro* investigation has shown progressive changes with age in intestinal ultrastructure, mucosal enzymes, and transport processes.² It is therefore possible that pre-term infants of differing gestational ages have different intestinal absorptive capacities and this could influence, for example, the definition of the ideal milk for these infants.

Infants who have intrauterine growth retardation (light for dates; LFD) need increased nutrients (per kg body weight) to promote catch-up growth. However, no systematic study of their intestinal absorptive capacity has been made. A recent preliminary study of rats with experimentally induced intrauterine growth retardation suggested that the small intestine was smaller, had fewer mucosal cells, and had a reduced lactase content compared with appropriately grown controls³. Absorption was not studied.

D(+) xylose absorption is widely used as a test of intestinal mucosal integrity.⁴ The usefulness of the one-hour blood xylose test in infants⁵ in detecting serial mucosal changes suggested that it could also be used to measure the maturation of the intestinal mucosa.

The purpose of the present study was twofold: to adapt the one-hour blood xylose test for use in neonates and then to use it to investigate intestinal absorptive capacity in low birthweight infants of different gestational ages and sizes.

Methods

Ethical permission for the study was received from Leicester Area Health Authority Ethical Committee. Informed consent was obtained from the infants' parents.

PATIENTS

Four groups of infants were studied in the Neonatal Unit and the lying-in wards at Leicester Royal Infirmary Maternity Hospital.

Group A—Full-term appropriate for dates infants—FTAfD

Group B—Pre-term appropriate for dates infants—PTAfD

Group C—Full-term light for dates infants—FTLFD

Group D—Pre-term light for dates infants—PTLFD

In this study the following definitions were used: term: 37-41 completed weeks of gestation; pre-term: less than 37 weeks; light for dates: less than 5th percentile allowing for gestational age, sex, birth order, and maternal height.

The feeding regime varied. Some infants received breast milk and some received a modified cow's milk formula. Overall, there was no difference between groups.

D(+) XYLOSE TEST

Dose of xylose

All patients were given 0.5 g xylose/kg body weight as a 10% (660 mmol) solution over five minutes, one hour before the next feed was due (no feeds were delayed or omitted). The reasons for choosing this dose are discussed later. One hour after the start of the test 0.2 ml of capillary blood was collected into a citrated microtube and stored at -20°C .

Route of administration of xylose

Oral An initial group of 18 group A infants

received xylose from a 50 ml feeding bottle with teat (Dinky Feeder) on the 6th day of life.

Transpyloric An additional 35 infants (15 group A, seven group B, five group C, eight group D) were given xylose by transpyloric infusion between the 2nd and 6th day of life. In 11 of these infants the test was repeated one to four times during the next seven to 15 days.

A 4 fg or 6 fg paediatric duodenal sonde with metal olive (Vygon 393-04 and 393-06) was passed into the stomach and its position checked by auscultation while 2 ml of air were injected; the stomach was then distended by 10 ml/kg body weight of air; with the infant in the right lateral position the tube was advanced slowly into the duodenum. When air could no longer be aspirated it was assumed that the tube was in the duodenum⁶ (see Discussion). The solution of xylose was steadily infused using a syringe pump (Havard 2620, TEM Crawley).

XYLOSE ASSAY

Xylose was assayed in whole blood by the method of Roe and Rice⁷, with the following modifications: after Somogyi deproteinisation, 10% 4 Bromo-alanine was added to duplicate samples which were incubated for 15 minutes at 70°C and the absorbance read at 475 nm on a Beckman 25 spectro-fluorimeter. A standard curve (0-33 mmol/l) was constructed for each assay.

STATISTICAL ANALYSIS

Results were compared using the paired Student's *t* test and were expressed as mean and standard error of the mean (SEM).

Results

All neonates tolerated the procedure well. ECG was monitored in 10 cases and Pa O₂ (Searle indwelling arterial catheter) in four. No changes were observed during the intubation or infusion.

ONE HOUR BLOOD XYLOSE AFTER ORAL ADMINISTRATION

The results for group A infants are shown in Fig. 1. The mean $\pm$ SEM was 0.98 ± 0.11 mmol/l with a range of 0.42-1.67 mmol/l.

ONE HOUR BLOOD XYLOSE AFTER TRANSPYLORIC INFUSION (Fig. 2)

Group A infants

The mean $\pm$ SEM was 1.41 ± 0.07 mmol/l with a range of 1.25-2.01 mmol/l. These results are significantly higher ($p < 0.01$) than in the oral group, and the range is narrower.

Fig. 1 One hour blood xylose in group A infants. Comparison of two routes of administration of 0.5 g/kg xylose ($\bar{x} \pm \text{SEM}$).

Fig. 2 One hour blood xylose after intraduodenal infusion in 35 infants of differing gestational age and size (for abbreviations see text).

Group B infants

The mean $\pm$ SEM was 1.17 ± 0.07 mmol/l (range 0.9–1.39 mmol/l).

Group C infants

The mean $\pm$ SEM was 0.73 ± 0.06 mmol/l (range 0.56–0.91 mmol/l).

Group D infants

The mean $\pm$ SEM was 0.96 ± 0.17 mmol/l (range 0.58–1.72 mmol/l).

There were significant differences between group A and all other groups (group B, $P < 0.05$; group C, $P < 0.001$; group D, $P < 0.05$); there was a significant difference between group B and group C ($P < 0.05$). Differences between group D and both groups B and C did not reach significance.

Fig. 3 Repeated one hour blood xylose tests in 11 infants, studied in the first three post-natal weeks.

SERIAL STUDIES OF 11 INFANTS (Fig. 3)

One group A, five group B, two group C, and three group D infants were studied two to five times between the 3rd and 20th day of life. The individual results are shown in Fig. 3.

The lowest initial results were seen in LFD infants. All groups showed a rise in serial values but the LFD groups (C and D) showed no signs of catch up by 3 weeks of age and some results appeared to fall further behind those of AFD infants.

Discussion

Investigations in neonates are limited by ethical and technical constraints. The present investigation was tolerated well by all infants and was accepted readily by all parents.

Tests of xylose absorption have been widely used to assess the integrity of the small intestinal mucosa.⁴ The one-hour blood xylose test can detect induced changes in the structure of the mucosa⁵, and this was the main reason for selecting it for use in the present study.

In previous studies using xylose many different dosage regimes have been used—for example, 25 g for an adult⁸, 15 g for all ages⁹, 5 g¹⁰ or 0.5 g/kg¹¹ for a child. The infants in the present study varied widely in size so that a graded dose seemed appropriate. The exact relationship between gut length, mucosal surface area, and body size is not known. The decision to vary the dose according to body weight was made on the grounds of practicality, and follows the recommendations of other workers.¹² Preliminary use of xylose in a dose of 1 g/kg induced diarrhoea in most infants. 0.5 g/kg was tolerated well and produced no symptoms, and was therefore used for the main study.

In the preliminary studies in which xylose was given orally, the one-hour blood xylose levels were low with a large range. Gastric emptying is erratic in the neonatal period and this may have influenced the results. In the main study xylose was infused distal to the pylorus and the mean for group A infants was significantly higher with a narrower range; the higher mean one-hour xylose levels after intraduodenal infusion are probably the result of increased amounts of the pentose reaching absorption sites during the test.

We studied three infants who had indwelling umbilical arterial catheters and monitored the blood xylose every 20 minutes for two hours. After intraduodenal infusion of xylose in each infant the blood xylose rose most quickly in the 40 minutes and reached a peak between 60–80 minutes. This suggests that the one hour blood xylose test may be justifi-

fiably used to compare xylose absorption in different infants.

The results in pre-term appropriately grown infants are significantly lower than in the full-term controls. There is overlap in the results of the two groups so that conclusions must be tentative. It is possible that these differences may be caused by a smaller mucosal surface area or diminished enterocyte function in pre-term infants.

There is a wide range of results in the light for dates infants. Most had low or very low one hour blood xylose levels, again suggesting diminished absorption or reduced enterocyte function. This concept is supported by the changes in the intestine that are induced by experimental intrauterine growth retardation.³ However, two group D infants had normal blood xylose levels. It is possible that the effects of immaturity or intrauterine growth retardation on gut function are variable in different individuals; changes in extracellular fluid volume may explain partly the wide variation in this group (see below).

Serial studies during the first 3 weeks of life showed increased xylose absorption in all groups, but the slowest rate of increase was seen in LFD infants. Some inappropriately grown infants fail to catch up in overall growth.¹³ It is not known whether the diminished intestinal function demonstrated in this study is part of this failure, and additional investigation is important.

In interpreting these data it is important to consider explanations for differences in one hour xylose levels other than variations in intestinal absorption. The known differences in volume of extracellular fluid in infants of different gestational age and size¹⁴ are insufficient to explain the differences between groups A, B, and C. There is considerable variation in extracellular fluid volume in pre-term infants who are inappropriately grown, and this may partly explain the wide variation in results in group D. Differences in bacterial flora in the intestine are unlikely to affect the one hour blood xylose result; Kendall and his colleagues have suggested that high concentrations of bacteria require longer than five hours of incubation to influence xylose levels.¹⁵ Little is known of the effect of immature renal function or the rate of xylose excretion, and this requires additional study.

The overall assimilation of nutrients is a complex process and the present investigations have explored only one aspect of proximal intestinal function. It will be necessary to study the absorption kinetics of other actively absorbed sugars as well as other nutrients in infants of differing gestational age and size, because the long-term nutritional implications may be considerable.

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