Correspondence

Necrotising enterocolitis. Increased incidence in infants receiving nasoduodenal feeding

Sir,

Beddis and McKenzie¹ discussed the possible role of nasoduodenal feeding (NDF) in the aetiology of necrotising enterocolitis (NEC). They did not find a significantly higher incidence of NEC in their group of infants fed by NDF compared with those not being fed by NDF. We should like to report our observations.

During a 2-year period (1978-9) we noticed an increased incidence of NEC. The total number of cases with NEC was 34, representing a rate of 0.94 per hundred admissions, which rose to a peak of 7.5 during the last 5 months of the period. 77 matched control infants were chosen retrospectively among those of similar birthweights and dates of admission. The following factors were compared: birthweight, gestational age, 1- and 5-minute Apgar scores, highest haematocrit, type of formula fed, daily volume and caloric intake, and incidence of respiratory distress, persistent patent ductus arteriosus, mechanical ventilation, sepsis, exchange transfusion, and prevalence and time of indwelling umbilical catheters. No differences were found for any of these parameters between the two groups by Student's *t* test or the χ^2 test. However, NDF had been used in 16 (47%) of the patients with NEC, and in 14 (18%) of the matched controls ($P < 0.01$).

The number of patients and controls fed by NDF in which this method was used electively—that is without trying other methods first—was similar (14 of 16 in those with NEC were being fed by NDF, and 12 of 14 of the controls were being fed by NDF). That means that only 2 babies in each group had shown a poor tolerance to a previous trial of gastric feeding. NDF was given via a Silastic tube, and the formula continuously administered by a constant flow infusion pump. In each case the position of the tube was confirmed by x-ray.

Although NEC has been quoted as a possible complication of NDF, a comparatively greater risk has not been reported. It remains to be determined whether changes in bacterial intestinal microflora in infants with a nasoduodenal tube in place,² which are similar to those found in NEC,³ may account for our observations. We suggest that although NDF has a place in the feeding of preterm newborn infants it should not be used as an initial standard method of feeding in nurseries, particularly if NEC is not uncommon.

References

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Dr McKenzie comments:

The figures presented by Vazquez *et al.* suggest that during a 2-year period there was an epidemic of NEC in the neonatal unit at a time when the admission rate was much below average (calculated from figures presented). More babies with NEC had been fed by NDF than matched controls without NEC. However, the indications for NDF are not clear; why were more babies of the NEC group fed by NDF despite being of the same birthweight and gestation as the controls? It would also be interesting to know if the increased incidence of NEC during the last 5 months of the study paralleled an increased incidence of NDF.

Although the figures are interesting and it is wise to draw attention to the probable change in upper intestinal flora which may accompany transpyloric intubation, I think that it would be difficult to incriminate NDF in the development of NEC from this retrospective study.

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Detection of carbamyl phosphate synthetase I deficiency using duodenal biopsy samples

Sir,

We read with interest the paper by Hoogenraad *et al.*¹ and should like to comment on it.

The authors stated that only one case of complete lack of carbamyl phosphate synthetase I (CPS I) had been reported but we can draw their attention to at least

4 others: a personal observation in 1977,² and papers by Sheffield *et al.* in 1976,³ Oberholzer and Palmer in 1976,⁴ and Mantagos *et al.* in 1978,⁵ all of which were published in journals in the English language.

The presence of CPS 1 activity in duodenal mucosa has been documented⁶ and in our case reduced CPS 1 activity in gut was found.² However, a duodenal biopsy during the neonatal period is technically difficult to perform without risk, and in the case related by Hoogenraad the biopsy was performed at 2 years of age. We agree that early diagnosis is important so a needle biopsy of the liver, taking the usual precautions, is probably the safest way to obtain tissue for enzymatic studies.

Our experience suggests that urinary orotic acid measurement is more helpful in diagnosis than was indicated by Hoogenraad. If the clinical presentation (normal delivery, short period without abnormal signs, neurological and digestive signs appearing when feeding is started) suggests an error of metabolism and if intense hyperammonaemia is noted without specifically abnormal amino-acid and organic acid patterns, ornithine transcarbamylase (OTC) or carbamyl-phosphate synthetase deficiencies should be considered. In such cases absence of orotic aciduria rules out OTC deficiency. This method of reasoning permits one approach to diagnosis, while waiting for a clinical improvement which will allow biopsies.

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Dr Hoogenraad and Dr Mitchell comment:

In reply to the letter by Farriaux *et al.* we acknowledge that there are a number of documented cases of complete lack of CPS 1, and we thank them for drawing this omission to our attention.

We hope our report has drawn attention to the potential of duodenal biopsy tissue assay for confirming the diagnosis of a number of urea cycle enzyme defects. We made no claim that any of the enzymes had not previously been assayed in the duodenum. In view of the lack of information about the safety of percutaneous liver biopsy compared with duodenal biopsy for establishing an early diagnosis, the choice of method will depend largely on the experience with each technique within the unit.

We agree with, and do ourselves use, the presence of a raised urinary orotic acid level as a valuable indicator of OTC lesions. However, other defects beside OTC lesions may produce orotic aciduria, and orotic aciduria may be absent in lesions other than CPS 1 defects—for example, defects in *N*-acetyl glutamate synthetase. Furthermore, there may be cases in which protein restriction began before full biochemical assessment. In such cases pyrimidine excretion patterns may be modified and no longer be typical of the underlying defect.

What to us appears to be of vital importance, both on clinical and genetic grounds, is the ability to identify carriers of urea cycle defects. In our experience, the measurement of orotic acid in urine after a protein load is a valuable and, perhaps, the best method for identifying carriers of OTC lesions.¹⁻² However, this approach will not detect CPS 1 carriers and our report shows the value of duodenal biopsy assay for heterozygous CPS 1 detection. Haan *et al.*² identified previously undiagnosed female carriers with partial OTC deficiencies using duodenal biopsy samples. In their report, and our own, nonproband carriers of OTC and CPS were noted to be not entirely asymptomatic and in fact had self-selected low protein diets to avoid disturbing symptoms.

References

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