

Parenteral nutrition compared with transpyloric feeding

E J GLASS, R HUME, M A LANG, AND J O FORFAR

Department of Child Life and Health, University of Edinburgh, Simpson Memorial Maternity Pavilion, Edinburgh

SUMMARY Fifty nine infants of birthweight less than 1500 g were allocated alternately to initial total parenteral nutrition or to transpyloric feeding. Mortality was similar between the two groups. Ten of the 29 infants in the transpyloric group failed to establish full enteral nutrition during the first week of life. No beneficial effects on growth were shown in infants receiving parenteral nutrition. Acquired bacterial infection was higher in the parenteral group and associated with morbidity and mortality. Conjugated hyperbilirubinaemia occurred only in the parenterally fed infants. The incidence of necrotising enterocolitis was higher in the transpyloric group. Parenteral nutrition does not confer any appreciable benefit and because of greater complexity and higher risk of complications should be reserved for those infants in whom enteral feeding is impossible.

Adequate nutrition of the very low birthweight infant is necessary both for immediate survival¹ and for optimal growth and development.²⁻⁴ It may be difficult to achieve these aims on feeding initially by the enteral route because of limitations imposed by an immature gastrointestinal tract and the respiratory effects associated with tube feeding.⁵⁻⁶ Some of the problems of enteral feeding may be overcome by delivering the milk feed beyond the pylorus.⁷ Total parenteral nutrition allows a higher caloric intake per unit volume of feed⁸ and avoids respiratory complications, but the technique is complicated and extensive biochemical and bacteriological monitoring is needed. Enteral feeds containing 85 kcal/100 ml are in common use in Europe, but few parenteral regimens achieve this energy density. Although there are many reports of the feasibility of total parenteral nutrition in preterm neonates, there have been few controlled studies comparing total parenteral nutrition with the enteral nutrition.⁹⁻¹⁰

We compared two groups of infants of birthweight less than 1500 g. In one group initial parenteral nutrition was followed by the gradual introduction of nasoduodenal feeding until full enteral feeding was achieved. Infants in the other group were fed transpylorically from birth, followed by nasogastric feeding (see below).

Patients and methods

Between January 1981 and January 1982 all infants of birthweight 750 to 1500 g admitted to the special care unit, Simpson Memorial Maternity Pavilion, Edinburgh within 24 hours of birth were entered into the study. The infants were allocated alternately to the parenteral or transpyloric groups on a rigidly observed basis uninfluenced by the initial clinical condition of the infant. More infants born elsewhere were included in the parenteral group (Table 1): this occurred solely by chance and without bias.

Transpyloric feeding was administered by a 5 FG silastic nasoduodenal tube (Vygon) and began when the tube was in position (confirmed radiologically). The optimum tube end site was the third part of the duodenum.⁷ Fresh expressed milk from the infant's own mother was used but if not available, SMA Gold Cap (Wyeth Laboratories) was substituted. Milk was infused continuously, beginning at 1 ml/hr and increasing by 1 ml increments at 6 hourly intervals. Supplementary intravenous dextrose electrolyte solution completed the infants' planned fluid requirements.

In parenteral group infants, intravenous feeding was by a central venous catheter inserted by a

Table 1 Initial parameters in infants in the parenteral and transpyloric feeding groups

	Parenteral group	Original transpyloric group	P value
No of infants	30	29	
Boys/girls	18/12	17/12	
Birthweight (g)			
Mean (SD)	1237 (196)	1280 (176)	NS
Range	765-1490	855-1490	
Gestation (weeks)			
Mean (SD)	29.5 (2.1)	29.7 (1.8)	NS
Range	26-34	26-33	
Apgar score, mean (SD)			
1 minute	4.7 (2.8)	4.9 (2.9)	NS
5 minutes	8.1 (1.7)	7.8 (2.0)	NS
Outborn/inborn	10/20	3/26	<0.05
Crown to heel length at birth (cm), mean (SD) (No of infants)	38.3 (2.7) (25)	39.4 (1.6) (25)	NS
Occipitofrontal circumference on 3rd postnatal day (cm), mean (SD) (No of infants)	27.1 (1.4) (26)	27.2 (1.3) (25)	NS

percutaneous technique.³ In systemic bacterial infection a peripheral line was used. During the first 12 hours infants received dextrose electrolyte solution alone; Vamin with glucose (KabiVitrum) was introduced at 12 hours and Intralipid 20% (KabiVitrum) at 24 hours. Thereafter these were infused in a 9:3:2 (dextrose electrolyte solution:Vamin with glucose:Intralipid 20%) ratio. Intralipid was not infused if there was evidence of systemic bacterial infection. Addition to parenteral solutions and the priming of tubing were carried out using sterile techniques in a room set aside for the purpose. All fluids, extension sets etc were changed daily. A 0.22 μ Micropore filter was incorporated into the circuit. Once the infant's clinical status was stable or respiratory distress settled, a nasoduodenal tube was passed and infusion of milk supplementary to parenteral feeding began at 1 ml/hr and remained at this level for two to three days. The volume was then increased by 1 ml increments daily for two to three days and then 12 hourly until planned fluid requirements were reached. In both groups drugs, blood, and blood products were administered by a separate peripheral venous line.

Planned fluid requirements in both transpyloric and parenteral groups began at 50 ml/kg on day 1 and increased by 25 ml/kg/day to 200 ml/kg, based on the infants' daily weight. An additional 25 ml/kg was given during phototherapy and further adjust-

ments made on the basis of the infants' state of hydration. Both groups were fed by intermittent hourly nasogastric feeding at 1600 g and subsequent progression to breast or bottle feeding was determined on an individual basis.

The growth parameters measured were weight, crown to heel length, and occipitofrontal circumference. Infants were weighed naked on admission then daily until discharge, using an integrated electronic balance (Mettler PS 15). Crown to heel length was measured on admission and weekly thereafter using a Harpenden neonatometer. The initial measurement of occipitofrontal circumference was taken on day three, repeated on day 8, and then weekly.

Statistical analysis of acquired bacterial infection was by Wilcoxon rank sum tests, mortality rates and number of outborn *v* inborn infants by 2 \times 4 contingency tables. All other statistical analysis was by Student's *t* test.

Results

Patients. Fifty nine infants were studied—29 in the transpyloric group and 30 in the parenteral. There were no differences between the groups (Table 1). Three infants were small for gestational age, two in the transpyloric group and one in the parenteral.

Ten of the 29 infants in the transpyloric group failed to establish full enteral nutrition during the first week of life and were given either partial or total parenteral nutrition (the failed transpyloric group). Two of these 10 infants developed hypoxia during the passage of the tube; four failed to maintain the tube in position; one developed acute renal failure; two developed necrotising enterocolitis and a third was treated as such on the basis of abdominal distension and blood in the stools, although radiological features were absent.

Idiopathic respiratory distress syndrome was present in 15 infants in the parenteral group and 14 infants in the transpyloric group—among the latter five failed to establish enteral nutrition during the first week of life. The number of infants ventilated was similar in the two groups.

Enteral feeding. Thirty six of the 59 infants studied established full enteral feeding. Infants in the transpyloric group began feeding during the first day of life at 1 to 22 hours (mean 9.9 hours). Enteral (nasoduodenal) nutrition in the parenteral group was begun between 1 and 26 days (mean 6.7 days). Establishment of full enteral feeding in the parenteral group ranged from 10 to 44 days (mean 20.7 days) and from 2 to 8 days (mean 4.9 days) in the

transpyloric group. The time to establish full enteral feeding in the failed transpyloric group was similar to that in the parenteral group.

The number of tubes passed in surviving infants was between one and 7 (mean 2.7). The most common reason for replacement of the nasoduodenal tube was spontaneous displacement or removal by the infant. Less frequently the tube was pulled up during oropharyngeal suction and on occasion snapped or became blocked.

Loose stools in four infants settled with temporary reduction in the volume of milk infused. Blood stained gastric aspirates in 6 infants were treated with the administration of 1 ml/hr milk nasogastrically, and in all the bleeding ceased within 24 hours. Aspiration of volumes of bile greater than 5 ml was not uncommon during transpyloric feeding, and one infant who had two episodes of bile aspiration needed ventilation on one occasion. No episode of milk aspiration was recorded.

Fluid and calorie intake. There was no difference between the groups in fluid intake during the first postnatal week, but during the second and third weeks fluid intake in the transpyloric group was greater than in the parenteral (Table 2). The mean caloric intake was greater in the parenteral than the failed transpyloric and transpyloric groups during the first week (Table 2), but during the second and third weeks the mean caloric intake in the transpyloric group was greater than in the parenteral and failed transpyloric groups.

Table 2 Comparative fluid and caloric intakes during the first four postnatal weeks in infants in the transpyloric (n=19), parenteral (n=30), and failed transpyloric (n=10) groups. Values are mean (SD)

	Parenteral	Transpyloric	Failed transpyloric	P value
Daily fluid intake (ml/kg/24 hours)				
Postnatal week				
1	170.1 (19.5)	161.6 (24.3)	164.7 (21.7)	NS
2	174.7 (25.3)	226.4 (14.7)	176.0 (33.8)	T v P<0.001 T v FT<0.001
3	171.2 (29.5)	221.7 (15.4)	182.1 (25.7)	T v P<0.001 T v FT<0.001
4	187.9 (40.7)	214.1 (20.8)	203.8 (19.8)	T v P<0.05
Daily caloric intake (kcal/kg/24 hours)				
Postnatal week				
1	105.5 (10.9)	95.8 (17.6)	86.1 (12.1)	P v FT<0.001 P v T<0.05
2	117.8 (24.3)	141.5 (10.2)	110.5 (18.7)	T v P<0.01 T v FT<0.001
3	120.0 (24.6)	139.9 (11.0)	114.4 (16.0)	T v P<0.01 T v FT<0.001
4	131.1 (25.5)	135.1 (12.4)	132.4 (11.2)	NS

T=transpyloric group; P=parenteral group; FT= failed transpyloric group.

Growth patterns. The timing of maximal postnatal weight loss was earlier in infants in the parenteral group than in the transpyloric and failed transpyloric groups (Table 3). There was no difference in the maximal postnatal weight loss between the groups of infants nor was there any difference in postnatal age at which birthweight was regained.

Growth was considered in infants who survived from birth until the expected date of delivery or time of discharge if earlier (infants transferred to other hospitals excluded). The average weekly gain in growth for each infant was calculated by dividing the difference between the measurements at birth and those at completion of the study by the number of weeks in the study. These comparisons are justified in that the gestational age at birth and the postconceptional age at last measurement (37–38 weeks) did not differ between the groups. There were no differences in the average gain in weight or crown to heel length but a marginally greater increase in occipitofrontal circumference was noted in the transpyloric than in the parenteral group (Table 3). During the third week the weight gain of infants in the transpyloric group was greater than the parenteral group (as the switch to enteral feeding in the parenteral group was in progress) and marginally greater than that of the failed transpyloric group.

Complications. During the study 20 infants died, 12 (40%) in the parenteral group and 8 (28%) in the original transpyloric group—four of whom failed to establish transpyloric feeding in the first week. Most deaths occurred during the first week and were usually caused by intraventricular haemorrhage.

Table 3 Growth parameters. The number of infants measured in each group until 37 to 38 weeks were parenteral (15), transpyloric (15), and failed transpyloric (6). Values are mean (SD)

	Parenteral	Transpyloric	Failed transpyloric	P value
No entering study	30	19	10	
Postnatal weight loss (%)	11.1 (4.5)	12.5 (4.0)	16.0 (5.2)	
Day maximal postnatal weight loss	3.6 (1.1)	5.1 (1.1)	5.3 (1.4)	P v T<0.001 P v FT<0.01
Regain birthweight (days)	10.5 (4.5)	12.5 (2.1)	12.0 (1.8)	
Weight gain (g/week)	135.7 (38.1)	149.1 (32.6)	128.7 (27.2)	
Crown to heel length gain (cm/week)	0.86 (0.21)	0.85 (0.25)	0.81 (0.09)	
Occipitofrontal circumference gain (cm/week)	0.66 (0.15)	0.77 (0.14)	0.76 (0.21)	T v P<0.05

P=parenteral group; T=transpyloric group; FT=failed transpyloric group.

There were four deaths during the fourth postnatal week in the parenteral group, three from septicaemia and one from chronic lung disease (Table 4).

The incidence of acquired bacterial infection was greater in the parenteral than the transpyloric group (Table 4). The principal organisms were *Escherichia coli* and *Staphylococcus albus*. There were 20 episodes of septicaemia among 30 infants in the parenteral group (67%), two among 19 infants in the transpyloric group (11%), and four among 10 infants in the failed transpyloric group (40%). Nineteen of the 20 episodes of septicaemia in the parenteral group and two of the four in the failed transpyloric group occurred during parenteral nutrition, and in 12 of these a central venous line was in situ. The incidence of septicaemia was one episode/21 days with a central line and 1/37 days with a peripheral line.

Three infants in the transpyloric group developed necrotising enterocolitis during the first week of life and a further infant was treated for suspected necrotising enterocolitis (Table 4). Another two infants in this group developed symptoms suggestive of necrotising enterocolitis at one month of age. One infant in the parenteral group developed necrotising enterocolitis on day 13, when 25% of fluids were being given nasoduodenally, and required surgical treatment, but all the other infants with necrotising enterocolitis were treated medically. There was one death in an infant who developed necrotising enterocolitis and acute renal failure.

Eight infants developed conjugated hyperbilirubinaemia after the first week of life—6 in the parenteral group and two in the failed enteral group (Table 4). A raised alanine aminotransferase activ-

ity was also noted in four of these infants. In all cases liver function reverted to normal.

Discussion

One third of infants allocated to the transpyloric feeding group failed to establish adequate enteral feeding during the first week of life. This was usually for technical reasons that might have been obviated, but other important causes were exacerbation of pre-existing respiratory distress and the development of necrotising enterocolitis. In general, no problem was experienced in the transpyloric feeding of infants who were already being ventilated.⁷

While there was no difference in the maximal postnatal weight loss between the two groups the time of maximal weight loss was earlier in the parenteral group. In contrast, however, to the findings of Yu *et al*¹⁰ that parenterally fed infants regained their birthweight sooner, no difference was noted between the groups in our study. This may be related to the timing of introduction of enteral feeding.^{9 10}

The use of total parenteral nutrition may prevent the maturation of the gut hormonal system.¹¹ It had been hoped that the more adequate initial caloric intake in the parenteral group could be combined with stimulation of the gut by gradual introduction of milk feeding, thus preventing the deterioration in growth pattern associated with the switch from parenteral to enteral nutrition. There is, however, no evidence from our study that this aim was achieved, although increased catabolism associated with acquired bacterial infection may have adversely affected growth in the parenteral group.

Because infants who failed to establish transpyloric feeding initially (failed transpyloric group) were among the sicker members allocated to this group, the transpyloric group had a selective advantage over the parenteral group, and this should be considered when longer term growth is compared. No differences in average weekly weight gain or crown to heel length were noted in comparing the three groups over the whole period. There was a greater increase in occipitofrontal circumference in the enteral group than in the parenteral over the study period. The timing of peak velocity of head growth may have influenced this finding since this is related to gestational age, with less mature infants having a later peak velocity. Impaired caloric intake and illness are, however, also known to affect head growth.^{12 13}

Sepsis, to which the preterm infant is particularly prone, is recognised to be the most serious complication of parenteral nutrition in paediatric

Table 4 *Complications*

	Parenteral	Transpyloric	Failed transpyloric	P value
No entering Deaths	30 12 (40%)	19 4 (21%)	10 4 (40%)	
No with infection	22	9	7	P v T<0.05
Pneumonia	13	7	5	
Septicaemia	20	2	4	P v T<0.01
Necrotising enterocolitis	1	6	—	P v T<0.01
Conjugated hyperbilirubinaemia	6	—	2	P v T<0.05

Infants with septicaemia may have had a coincidental meningitis or pneumonia. Three of the cases of necrotising enterocolitis in the transpyloric group were suspected clinically but had either equivocal radiological features or none.

patients.¹⁴ Acquired bacterial infection occurred in two thirds of the infants in the parenteral group. An incidence of 0–50% has been recorded in various series.^{3 16} Sondheimer *et al*¹⁵ considered sepsis to be almost inevitable in the very low birthweight infant receiving parenteral nutrition. Septicaemia has been reported less commonly in infants receiving peripheral parenteral nutrition¹⁶ and strict attention to asepsis decreases the risk of acquired bacterial infection during parenteral nutrition. Hepatic dysfunction, which is known to occur during parenteral nutrition,¹⁵ developed in 8 of our infants and a striking temporal relation with infection was noted.

Necrotising enterocolitis was diagnosed in five transpylorically fed infants and suggestive symptoms and signs were present in one other. The infants studied were a high risk group for the development of necrotising enterocolitis, which can be related to the onset of milk feeding.¹⁷ A high fluid intake is associated with an increased risk¹⁸ and three infants developed symptoms during the first weeks of life, at which time the fluid intake was relatively high. The role of different types of enteral feeding in the aetiology of necrotising enterocolitis is unclear, as the disorder occurs not only in infants fed transpylorically but also in those fed nasogastrically.¹⁰

Parenteral feeding does not confer any significant benefit and because of the greater complexity of parenteral feeding and the serious risk of complications, we consider that it should be reserved for those infants in whom enteral nutrition is impossible. We do not agree with those authors who advocate that enteral nutrition be withheld from infants of less than 1500 g birthweight for 2 to 3 weeks in order to prevent necrotising enterocolitis¹⁹ without consideration of other risks involved.

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Correspondence to Dr R Hume, Department of Child Life and Health, Simpson Memorial Maternity Pavilion, Lauriston Place, Edinburgh EH3 9EF.

Received 7 November 1983