A Comparison of Oral Feeding and Total Parenteral Nutrition in Infants of Very Low Birthweight

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SUMMARY

A controlled trial of total parenteral nutrition (TPN) was conducted in 86 infants weighing less than 1 500 g. There was no significant difference in neonatal mortality and morbidity between those receiving TPN and the controls who were fed 'humanised' milk by continuous nasogastric drip. There was an over-all reduction in neonatal mortality for which modern intensive care techniques and skilled nursing care were largely responsible. A place for TPN exists in the management of the sick, low birthweight infant, where feeding by oral route is contra-indicated and nutritional support is temporarily desired. The adaptation of this important technique to low birthweight infants is discussed.

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The neonatal mortality and morbidity of infants of very low birthweight remains high.[1-3] In 1971 in Cape Town, the mortality for infants weighing less than 1 000 g at birth and for those between 1 000 and 1 499 g was 90% and 51% respectively. Of greater concern is the high incidence of mental and motor handicap reported in such infants.[4-6]

One of the possible reasons for the developmental handicap is the problem of providing adequate nutrition after premature delivery. The practice of initial fasting has been replaced by early high caloric feeding. Early provision of energy and nutrients can favourably influence both motor and mental development of the low birthweight infant.[7,8]

More recently, total parenteral nutrition (TPN) has been shown to be capable of supporting growth in children and newborn infants.[9] Theoretically, TPN can bridge the gap between the placental environment and postnatal alimentary function.

In 1972 a clinical trial of the feeding of infants of less than 1 500 g birthweight was started in Cape Town. The aim was to compare oral feeding with TPN in infants receiving modern intensive care. This article outlines the management, methods of feeding and the early outcome of the 86 infants studied.

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PATIENTS AND METHODS

Infants with birthweights from 500 to 1 500 g born at Groote Schuur Maternity and Peninsula Maternity Hospitals, who showed no evidence of hyaline membrane disease, congenital abnormalities or other apparent illness at birth, were included in the study. The 86 infants were divided into 'oral' and 'parenteral' groups by random selection. The gestational ages of the infants were determined by the physical and neurological criteria of Dubowitz.[10] Table I shows the distribution for weight, gestational age, sex and assessment of intra-uterine growth of the two groups.

TABLE I. DETAILS OF INFANTS STUDIED

	Oral	Parenteral
Number (total)	43	43
Males/females	22/21	22/21
Weight (g)		
Mean ± 1 SD	1 293,5 ± 173	1 235,6 ± 235
Range	550 - 1 500	800 - 1,500
Gestational age (weeks)		
Mean ± 1 SD	30,8 ± 2,3	30,8 ± 1,9
Range	26 - 36	26 - 34
Number small for gestational age	9	5
Number appropriate for gestational age	34	38

There was no significant difference between the two groups ($P>0,05$).

Routine Management for the First 24 Hours (Both Groups)

After delivery, the infant was placed in a single-walled Drager incubator with a temperature setting of 34 - 35°C. Skin temperature was recorded by an electrode (Telethermometer) and was maintained between 35,5 and 36°C.

Trained nursing staff recorded vital signs every 15 - 30 minutes and measured hood oxygen concentrations (when in use) with Beckman analysers. Heart rate was monitored by a signal oscilloscope. The occurrence of apnoea was detected by placing the infant on a Lewin Apnoea Alarm mattress.

Immediately after birth, swabs were taken from the umbilical stump and ear, and sent for bacteriological

examination. A nasogastric tube was passed and the gastric aspirate examined for pus cells, and cultured. The placenta was sent for histology. Samples of blood were taken for biochemical determinations. The serum bilirubin was estimated daily (Bilirubinometer; American Optical Co.), and continuous phototherapy initiated when bilirubin levels rose above 6 mg/100 ml. Acid-base determinations were performed and acidosis corrected with intravenous sodium bicarbonate.

No oral feeds were given for the first 24 hours. A 10% invert sugar solution (60 ml/kg/day) was commenced 2 hours after birth, first by scalp vein infusion and thereafter at 6 - 12 hours by umbilical arterial catheter (Argyle 3,5 Fr., Aloe Medical). The catheter was advanced, using sterile technique, to a distance of 10 - 12 cm, to lie in the descending thoracic aorta. Its position was checked by roentgenography at the cotside. No dressings, sutures or antibiotic ointments were applied. The catheter was secured by a transverse H-type adhesive strap. The umbilical stump was cleaned with 70% alcohol every 6 hours and allowed to dry. Intra-arterial fluids were infused through this catheter by a continuous infusion pump (Ivac Model 501). In 3 infants the umbilical artery could not be cannulated and the TPN was given by peripheral scalp vein.

Antibiotics were not given as a routine. If the gastric aspirate showed the presence of more than 5 pus cells per high-power field, or if organisms were cultured from the gastric aspirate, penicillin and kanamycin in appropriate doses were given by intramuscular route.

At 24 hours oral or parenteral feeding was commenced.

The oral group were fed full-strength 'humanised milk' (Nan; Nestlé) by continuous intragastric drip, according to the schedule in Fig. 1. The small volumes of milk for the first 3 days were supplemented with intravenous 10% invert sugar. The maximum energy intake of 664 kJ (166 kcal)/kg/day at maximum volume intake of 200 ml/kg/day was planned to be reached by day 5, but it was usually achieved later in the infants with extremely low birthweight. The feeds were supplemented by 1 g sucrose to every 30 ml formula.

The nasogastric feeding tube was positioned according to the technique described by Ford.[11] Milk feeds were infused through a Pedatrol (Baxter), graduated in 10-ml sachets, which was connected to the nasogastric feeding tube. Gastric aspiration was at first carried out as a routine before feeding, but was found to be unnecessary since the residue of milk in the stomach was invariably found to be minimal.

The umbilical arterial catheter was removed on the 4th day.

The parenteral group received oral feeds for 10 days, but were given parenteral fluids by continuous arterial perfusion according to the schedule in Fig. 2. Beginning at 24 hours, the system employed for the administration of the parenteral fluid was set up as shown in Fig. 3.

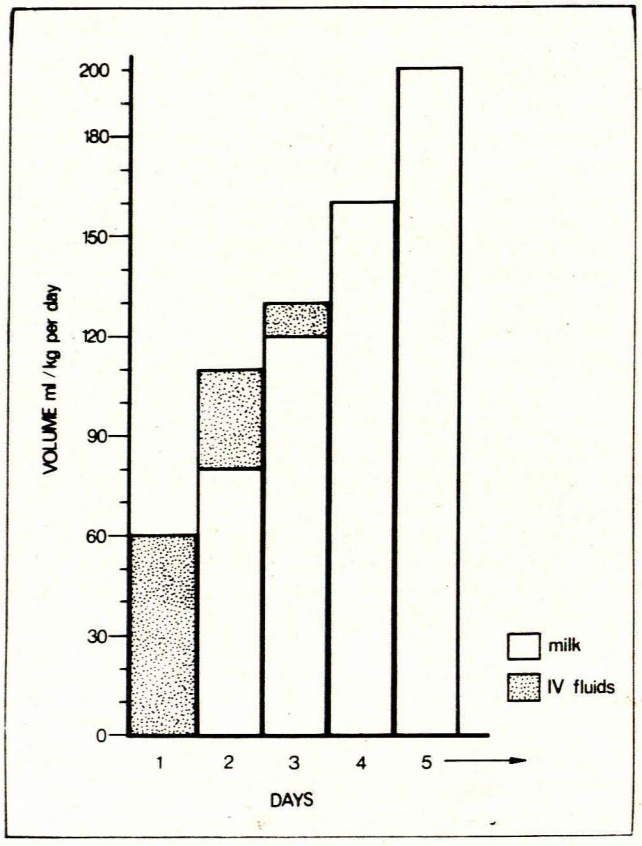

Fig. 1. Daily nasogastric (oral) feeding schedule.

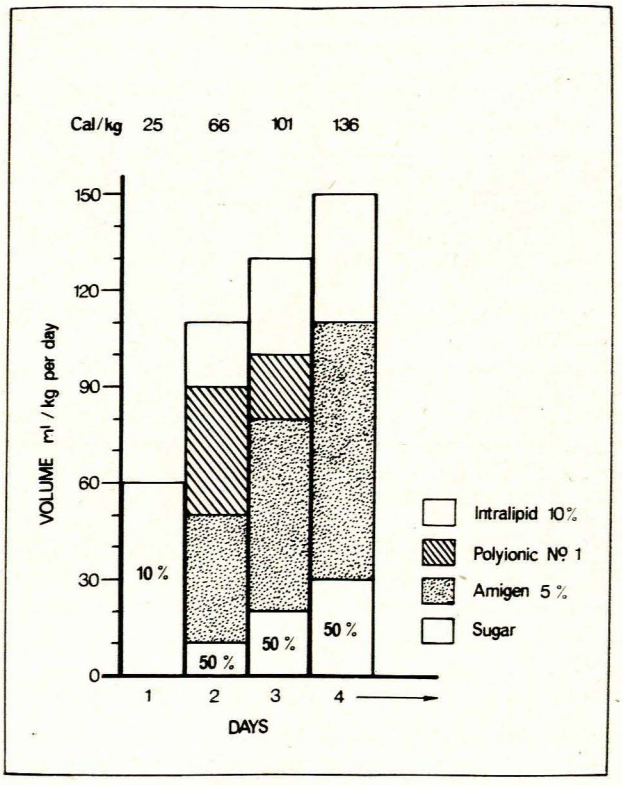

Fig. 2. Daily parenteral infusion schedule.

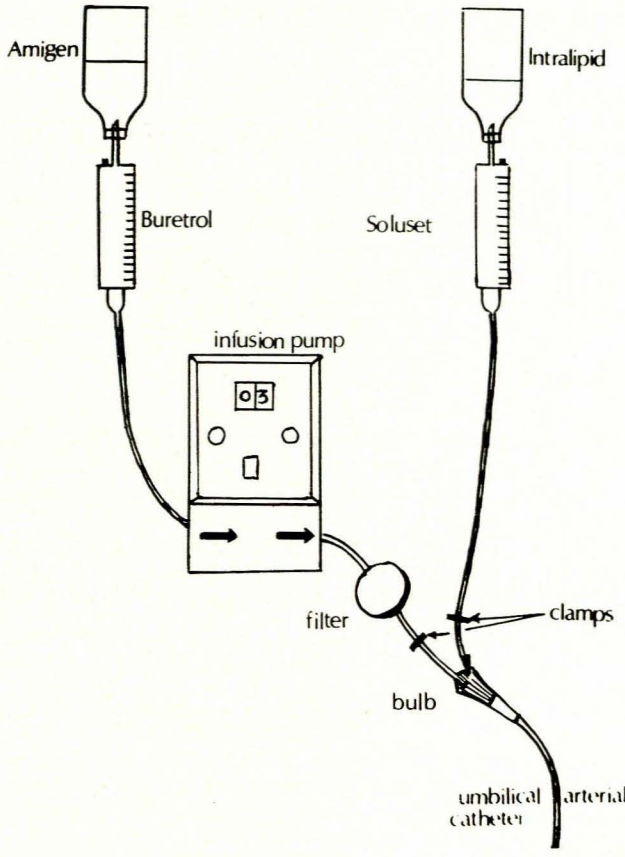

Fig. 3. Arrangement for total parenteral nutrition infusion. Note the incorporation of a final flow filter (Baxter Laboratories) but direct infusion of Intralipid.

On the 2nd and 3rd days, the fluid was diluted with a maintenance solution (Polyionic No. 1; Baxter) to avoid hyperglycaemia, glycosuria, hyperosmolality and dehydration.[12,13] Maximum concentration and volume (150 ml/kg/day) was reached on the 4th day. The volume, energy content and constituents of the standard parenteral solution are shown in Table II.

The entire system (apart from the arterial catheter) was changed daily. The Intralipid was run over 5 hours during the morning, and the Amigen/dextrose solution followed over 19 hours during the afternoon and at night. TPN was maintained until the 10th day, after which oral milk feeds (Nan; Nestlé) were started in the same manner described for the oral group. At this stage the volume of the parenteral fluid was decreased to supplement the increasing volumes of milk. The catheter was removed on the 14th day by clamping and withdrawal in stages over 2 hours.

Repeated cultures were taken from the infusate. Dextrostix (Ames) estimations were done every 8 hours for the first 5 days of TPN to detect hyperglycaemia. Urinary glucose estimations were done daily for the first 5 days by Clinitest tablets (Ames) and random checks were made thereafter.

A comparison of the solutions used appears in Table III. It will be noticed that the milk contained a higher water, carbohydrate, fat and ash content than the parenteral solution. The milk plus added sucrose being given orally was probably not directly comparable with the parenteral infusion.

From 14 to 28 days both groups received routine milk feeding and nursery care.

TABLE II. PARENTERAL NUTRITION SOLUTION

	Volume (ml/kg/day)	Calories (cal/kg/day)
Fat emulsion*	40	44
Casein hydrolysate†	80	32
50% Dextrose water	30	60
Total	150	136 (3,64 kJ/ml)

Additions: 20 ml plasma/kg weekly (trace elements)
Folic acid 1 mg daily‡
Vit. B_{12} 10 μg weekly¶
Multivitamin infusion§ 0,3 ml daily

Final intake (per kg/day)	Infusion rate
Fat 4 g	0,8 g/h over 5 hours
Protein 3,2 g	0,17 g/h over 19 hours
Carbohydrate 19 g	1,0 g/h over 19 hours
Sodium 2,8 mEq/l	
Potassium 1,6 mEq/l	
Chloride 1,6 mEq/l	
Calcium 0,8 mEq/l	
Phosphate 2,4 mEq/l	
Magnesium 0,2 mEq/l	
Water 123 ml	

* Intralipid 10% (Vitrum, Sweden).
† Amigen 5% in dextrose 5% w/v (Baxter Laboratories).
‡ Folvite (Lederle).
¶ Cytamen (Glaxo-Allenburys).
§ Pancebrin (Lilly).

TABLE III. COMPARISON OF NUTRIENT SOLUTIONS

	Oral (per kg/day) (Nan; Nestlé)	Parenteral (per kg/day) (Amigen/dextrose/ Intralipid)
Volume	200 ml	150 ml
Carbohydrate	20,6 g	19 g
Protein	3,2 g	3,2 g
Fat	6,8 g	4,0 g
Water	169 ml	123 ml
Calories	664 kJ (166 kcal)	544 kJ (136 kcal)
Minerals	0,6 g	0,275 g
Vitamins	A, B, C, D, E* Folic acid Iront	A, B, C, D‡ Folic acid Iront (oral)

* Vidaylin drops (Abbott).
† Ferrodrops (Parke Davis).
‡ Pancebrin (Lilly).

RESULTS

General

No difficulties were experienced by the nursing staff in the execution of either method of nutrition. The acquisition of a number of constant infusion pumps made administration of both the milk and the parenteral solutions easy and accurate. Although heparin was not included in the parenteral solution, catheter blockage was an infrequent problem. When it occurred the catheter was replaced.

Few problems were encountered with the oral milk feeding technique. Vomiting occurred either as the result of an improperly positioned nasogastric tube or as an indication that the infant was infected.

With the slow daily increase in concentration of the parenteral solution, hyperglycaemia was rarely found, and glycosuria, when encountered, was insignificant (less than 1% of glucose infused).

Repeated cultures of the parenteral infusate were negative, despite the fact that the solution was mixed at the bedside. The administration technique shown in Fig. 3 proved simple and satisfactory.

Mortality and Morbidity

The mortality for the oral group was 14% (6/43 infants) and for the parenteral group 20% (9/43 infants). The difference was not statistically significant ($P>0,05$). Despite the reduction in mortality, the neonatal morbidity rate remained high in both groups, and was a constant problem in the management of these infants. Of the 86 babies only 38 had no clinical complications. Table IV shows the incidence and distribution of complications and the causes of death in the two groups.

Pneumonia, septicaemia (diagnosed on positive blood culture), recurrent apnoea and enteritis (including necrotising enterocolitis) emerge as the commonest forms of morbidity. One infant died of congenital pneumonia. Pneumonia, notoriously difficult to diagnose early in the preterm infant, was often detected after an apnoeic attack. Septicaemia was more often related to an infected environment (prolonged rupture of the membranes, presence of large numbers of pus cells in the gastric aspirate and histological evidence of placental infection) than to catheter placement.

Of the 15 infants who died, only 1 was of more than 30 weeks' gestation. Seven of the infants were males and 8 were females. The mortality rate below 28 weeks' gestation was 83% and between 28 and 30 weeks' gestation it was 43%.

TABLE IV. MAIN CLINICAL COMPLICATIONS AND CAUSES OF DEATH IN INFANTS STUDIED

	Oral		Parenteral		Total	
Complication	Alive	Died	Alive	Died	Alive	Died
None	22	0	16	0	38	0
Pneumonia	5	1	3	2	8	3
Septicaemia	4	1	3	1	7	2
Enteritis	1	1	3	0	4	1
Catheter problems	0	0	4	0	4	0
Recurrent apnoea	5	2	5	3	10	5
Intracranial haemorrhage	0	1	0	2	0	3
Unexplained death	0	0	0	1	0	1
	37	6	34	9	71	15

Apnoea

The incidence of apnoea during the first 10 days (cessation of breathing for more than 30 seconds with change in skin colour and bradycardia) was 37% and was a frequent sign of pathology, and the mortality rate in infants who had apnoeic attacks was significantly higher than in those who had no attacks. There was no statistical difference in incidence of apnoea between the oral and parenteral groups.

Growth

There was no significant difference in the rate of growth between the oral and parenteral groups as judged by weight, length and head circumferences. The growth curves for appropriate-for-gestational-age (AGA) infants followed the 25th percentile. No single parameter was superior to the others as a criterion of the rate of growth. Postnatal growth was unable to match intra-uterine growth. In small-for-gestational-age (SGA) infants, all three parameters were below the 10th percentile. The daily rate of growth in head circumference was the same for AGA and SGA infants (0,10 cm/day). The mean daily weight gain for both groups was 21,2 g/day. The mean daily gain in length was 1,24 mm for the first 6 weeks.

Birthweight was regained by the 6th day in both groups. On this day the mean caloric intake was 520 kJ (130 kcal) and 516 kJ (126 kcal)/kg for the oral and parenteral groups respectively. This caloric intake appears to be the minimal caloric requirement for initial weight gain.

Biochemistry

A full report of the serum and urine chemistry and plasma amino acid determinations will be given in a future publication. During TPN the values for serum sodium, potassium, chloride, calcium, phosphate, blood urea, serum osmolality, total protein, albumin, globulin and serum glutamic oxalo-acetic acid transaminase (SGOT) were all within normal limits. There was also no significant alteration in acid-base balance, nor was there an increase in the incidence of hyperbilirubinaemia.

However, during the 10-day period of TPN there was a persistent elevation in serum cholesterol levels above the

normal range for infants. In addition, there was a general increase in the concentration of plasma amino acids during TPN. In particular, the levels of aspartic acid, cystine, glutamic acid, isoleucine, leucine and phenylalanine were significantly elevated above corresponding levels determined during milk feeding in the oral group. Plasma amino acid levels returned to normal when TPN was discontinued.

DISCUSSION

Preterm infants have very small hepatic glycogen reserves or protein resources[14] and with conventional feeding it may take from 8 to 17 days to reach caloric and protein requirements.

Numerous reports of the management of low birthweight infants with TPN have recently appeared in the literature.[13-21] To date, the only controlled trial of intravenous alimentation in low birthweight infants has been reported by Bryan *et al.*[22,23] They, however, supplemented the TPN with oral milk. They also found no difference in mortality between the two groups.

The umbilical artery is available for cannulation only in the newborn, and offers a route of administration which, in our experience, results in an acceptably low incidence of complications (7,8%). This has also been found by others.[24-26]

The administration of simple intravenous sugar solutions does not result in weight gain.[27,28] It would be attractive to postulate that since an increased amount of energy is being given earlier by TPN, the positive weight gain is due to utilisation of amino acids for protein synthesis, and that the infants are achieving positive nitrogen balance.

The minimal change of biochemical parameters is remarkable. Elevations in blood urea have been reported and probably reflect the increased nitrogen intake.[22]

TPN did not appear to alter bilirubin metabolism, and phototherapy was responsible for the maintenance of bilirubin levels within safe limits in both groups.

Serum osmolality was within the normal range owing to the fact that the rate of infusion was constant and slow.[9] Providing the same protein intake for each group resulted in similar serum protein levels during the first month.

Intralipid has been used in low birthweight infants[16] and the maximal removal capacity of fat from the intravascular compartment in low birthweight infants has been found to be in the normal range for adults.[29] Despite this, Duncan and Usher, also using 4 g/kg/day,[17] reported elevated cholesterol levels but no persistent hyperlipaemia. Our findings substantiate this.

The majority of complications arose as a result of infection. The gastric aspirate provided an important clue to the presence of an infected environment and helped us to use antibiotics discriminately. Histology of the placenta provided further evidence of perinatal infection. We have found a positive correlation between these two parameters and mortality.

A surprising finding was that recurrent apnoea was as frequent in TPN as in oral feeding. This rather supports the concept that this is due to central nervous immaturity and not related to feeds.

CONCLUSIONS

There was no statistical difference in gross mortality and morbidity between oral and parenteral feeding groups in our study. Whether TPN improves the ultimate quality of these infants in later years remains to be seen, and a prospective study is in progress.

TPN has been established as an effective alternative to oral feeding in low birthweight infants. The indications for the use of TPN in the newborn period would include septicaemia, necrotising enterocolitis and respiratory distress (particularly during prolonged mask or nasal ventilation), when oral feeding is hazardous and metabolic demands are even greater than those of the 'well' baby.

The findings indicate that with limited resources, much can be achieved in the care of these tiny infants by good nursing and careful nasogastric feeding, without the more sophisticated parenteral feeding.

TPN is more laborious and requires great attention to detail and good nursing support. It should be restricted for the present to centralised neonatal care centres.

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