

# In VLBW infants in the first 48 hours of life is IV fluid safer than enteral feeding?

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**This review addresses the question:** *In VLBW infants in the first 48 hours of life is IV fluid safer than enteral feeding?*

The WHO Pocketbook of Hospital Care for Children recommends that if possible for babies with birth weight below 1.75 kg to give IV fluids at 60 mls/kg/day for the first day of life. If the baby is well and active then give 2-4 mls of EBM every 2 hours through a NG tube depending on the baby's weight. Feeding properly should be started when the condition of the baby is stable and only if there is no abdominal distension or tenderness, bowel sound are present, meconium passed and no apnoea. (Pocketbook chapter 3.10.3, page 54).

## INTRODUCTION

Prematurely born infants have complex nutritional needs to achieve optimal growth. The medical complications in these infants include respiratory distress, hypoxia, hypercarbia, hypotension, infection, acidosis, immature renal function and physiological gastrointestinal immaturity. The gastrointestinal immaturity is reflected in decreased gastrointestinal surface area, gastrointestinal dysmotility and delayed enzyme expression, which impose extra burdens on the system. There are additional concerns of aggressive feeding induced gastrointestinal mucosal injury, feeding intolerance (FI) and necrotizing enterocolitis (NEC). Due to all these factors as well as limited body energy stores and increased energy expenditure very low birth weight infants often receive parenteral fluids from soon after birth. Another approach is to give early enteral feeding which may reduce the risk of infection but may carry an increased risk of NEC and feeding intolerance.

This review intends to address the following question: In VLBW infants in the 1st 48 hours is IV fluid safer than enteral feeding?

## METHODOLOGY

The search engine used was PubMed and the clinical search strategy utilized was as follows: intravenous fluids, enteral feeding during first 48 hours of life, very low birth weight infants. Using the clinical filters for both therapy and broad specific, no article was found. The search was then broadened to

intravenous fluids and enteral feeding in very low birth weight infants under which one article was found.

Utilizing related articles links to this about 360 articles were found. All abstracts were read and those with no relevance to the topic were excluded. Those, that were considered relevant, were included for review and the complete article was sourced.

## RESULTS

Only one RCT compared parenteral and enteral feeding before the first 48 hours of life in very low birth weight infants (BW < 1500 g, VLBW) [1]. Other articles did not focus on the first 48 hours or used enteral feeding only after 48 hours of life. Troche et al performed a randomized controlled trial in which 29 mechanically ventilated VLBW infants were randomly assigned to receive only intravenous nutrition (NPO group, n=13), or 1ml/kg/hour of breast milk or formula (Similac special care, Ross laboratories) continuous feeding beginning at 24 hours of life in addition to total parenteral nutrition (early feeding group, n=16) [1]. Standard enteral feeding was begun in both groups at the resolution of the acute phase and advanced according to their protocol. The two groups were comparable in terms of birth weight, gestational age and Apgar scores. The early feeding group took fewer days to reach 120 ml/kg/d of enteral intake (10 +3 days compared to 13 + 4 days in NPO group; p< 0. 05). On day of life 30 early feeding group was 223+ 125 g above birth weight compared to 95 + 161 g in NPO group (p< 0 .05). The serum levels of somatostatin C and diamine oxidase and incidence of NEC or feeding intolerance did not differ between the two groups.

Dunn et al performed a randomized controlled trial (1988) in VLBW infants comparing early formula (½ strength Enfamil premature formula, Mead Johnson Laboratories) feeding starting at, but not before 48 hours of age, to a late feeding group which was NPO for at least DOL 9. They found that early feeding group had a beneficial effect on cholestasis jaundice, indirect hyperbilirubinemia, and metabolic bone disease [2].

Davey (1994) in a randomized controlled trial analyzed 60 < 2000 gm infants under 2 groups- early feeding (median age 2 days, n=29, initiated with 2-5 ml every 2 hours of ¼ strength premature formula, the concentration and volume thereby increased according to birth weight) and late feeding group (median age 5 days, n=31, rate of increase and volume same as early feeding group) [3]. The early group received fewer days of parenteral nutrition, lesser sepsis evaluations and percutaneous central venous catheters. The day of life to regain birth weight, days to achieve full feeding, duration of phototherapy, age at discharge, gastric residuals, withholdings of feeding, abdominal

distension or grossly bloody stools did not differ between the two groups. In this study however, the DOL when feeding was started was reported as median, therefore several infants received first feeding after 48 hrs of life.

McClure in 2000 performed a randomized controlled study including 100 infants and confirmed the findings of Troche et al, but these infants weighed up to 1750g and their feeding was started on DOL 3 [4]. They used breast milk and Nutriprem (Cow and Gate Nutricia) in their study.

Kennedy reviewed literature on early vs. delayed feeding in low birth weight infants. None of the studies described in this review included infants who were fed before 48 hours of life exclusively [3]. Effects of rate of advancement of feeding on NEC was studied by Anderson et al who suggested not to increase feeding by more than 20 ml/kg/d to avoid NEC [5]. Its validity was tested by another randomized controlled study which compared 15 ml Vs 35 ml advancements of Similac special care formula and found no difference in NEC [6]. However, increment by 20 ml/kg/d is an acceptable and widely followed feeding practice in VLBW infants.

Some believe that early enteral feeding may actually decrease the incidence of FI or NEC in VLBW infants by promoting gastric maturation. [7]. Slagle et al in a RCT compared the effectiveness of enteral feeding with breast milk or Enfamil premature formula, begun at DOL 8 vs. DOL 18 and reported that infants who received nutrition sooner had fewer incidences of feeding intolerance and achieved full enteral nutrition faster [8].

Berseth et al in a RCT have shown that the incidence of NEC is lower in infants who are < 32 weeks of gestational age and are fed in small volumes in early life [9]. The DOL when feeding was begun was decided by the neonatologist in this study and did not necessarily take place within the first 48 hrs of life. This study compared two groups. One was given 20 ml/kg/day of unfortified breast milk or Enfamil premature formula 24 for 10 days. The other group received the same nutrients but in increments of 20 ml/kg/day for 10 days. Five out of the eight infants who develop NEC in this study were fed breast milk.

## DISCUSSION

Despite an extensive literature search no study was identified which compared enteral feeding and IV fluids strictly in the first 48 hours of life in the VLBW infants.

NEC is inversely, and strongly related to gestational age and enteral feeding although it's exact pathogenesis is unknown [7,10]. It is also postulated that exposure to various pathogens of the infant's immature gut during the feeding process, and not feeding itself, predisposes to NEC

These concerns led to prolonged withholding of feeding in sick premature infants, which subsequently resulted in relative atrophy of gut mucosa [7]. Trials examining early feeding ensued. A systematic review of such published trials suggested that early introduction of feeding may shorten the time taken to achieve full feeds, decrease length of stay (LOS) and may not increase the risk of NEC [3].

Although not conclusively proven, during first 48 hours of life even low volume feeding may be hazardous and predispose to feeding intolerance and NEC in VLBW infants. Considering this, total parenteral fluid and nutrition is suggested in critically sick VLBW infants during the 1st 48 hours of life. In not so sick infants low volume feeding with ½ or ¼ strength premature formula or breast milk may be considered if available. Sick

infants are those who have moderate to severe respiratory distress, frequent oxygen desaturations, acidosis, significant patent ductus arteriosus, hypotension requiring inotropic support, hypoxic ischemic encephalopathy, hydrops, hypernatremia (serum Na > 145 meq/L), polycythemia (hematocrit > 65% and symptomatic), severe thrombocytopenia (< 100,000/mL<sup>3</sup>), confirmed or highly suspected sepsis, electrolyte imbalances e.g. significant hyponatremia (< 130 meq/L), hypo / hyperkalemia (serum K level < 3 meq/l and >6.5 meq/l), hypo/ hypercalcemia (serum Ca level < 7 & > 11.5 meq/L), hypermagnesemia ( serum level > 3 mg/dL), hyperglycemia ( serum glucose level > 140 mg/dl), severe anemia ( hematocrit < 30%), neutropenia ( ANC < 1500 mL<sup>3</sup>), excess fluid retention etc.

Suggested volume of total fluids in VLBW infants on day of life 0 (< 24 hours of life) is 80-120 mL/kg/day.[11] Extremely premature infants, especially those who are < 700 g at birth can be started at 100-120 ml/kg/d as they have very high cutaneous insensible water losses which may lead to hypernatremia very quickly.[12] Hypernatremia is a risk factor for intraventricular-periventricular hemorrhage and NEC, esp in an enterally fed infant. Infants who are around 1000 g can be started at 90-100ml/kg/d and larger infants at 80-90 ml/kg/d depending upon the degree of their skin cornification, which can be evaluated clinically. Total fluid intake should be adjusted daily according to the body weight, serum Na level and to some extent blood pressure. Serum electrolytes should be monitored very closely in all these infants. The constituents of parenteral fluid on DOL 0 (< 24 hours of life) should be dextrose ( in the concentrations of 5% in < 700 g, 7.5% in 700-1000 g and 10% in > 1000 g infants) with calcium in the doses of 100-200 mg/kg/d. 11 If possible intravenous protein in the doses of 1-2 g/kg/d may be provided on DOL 0.11 The protein intake should be increased by 0.5 to 1 g/kg/d and lipids should be added beginning with 1-2 g/kg/day in the parenteral nutrition by DOL 1.11 The maximum intake of protein and fat in the parenteral nutrition should be at 4 g/kg/day and 3 g/kg/d respectively.[11] The renal functions, occurrence of metabolic acidosis, severity of lung disease and hyperbilirubinemia, serum triglyceride levels and the presence of infection determine the rate of increments of parenteral protein and fat intake during the first week of life. The daily increments should be such as to allow 10 %-18% of body weight loss during the first 1-2 weeks of life. The lower the gestational age and birth weight, the higher % of body weight is physiologically lost, and the peak loss as well as the regaining of birth weight occurs later in life. In order to avoid overhydration and related complications, such as PDA, bronchopulmonary dysplasia and possibly NEC and intraventricular/periventricular hemorrhage, serum Na should be maintained within normal limits, preferably between 140-145 meq/L level. Once the birth weight is regained after appropriate physiological body weight loss, fluids can be liberalized generally by 10-20 ml/kg/d.

Enteral feeding can be initiated on DOL 0-1 in relatively stable VLBW preterm infants who weigh > 1000 g, and have no ventilator support need, are on minimal positive distending pressure with minimal to none lung disease and do not suffer from the earlier mentioned complications. In these cases initial volume of enteral nutrition should be 10-20 mL/kg /day and thereafter can be increased by 10-20 mL/kg/day to a total of 140 mL/kg /d within a week or two as tolerated. In ELBW infants ( birth weight < 1000 g) trophic or gut priming feeding, with preferably mothers breast milk or with preterm formula, can be started at <10mL /kg /d within first 48 hrs of life if the infant is stable on low ventilator support, has no desaturations or any of the above mentioned complications and preferably no indwelling umbilical catheters. This gut priming feeding can be

continued until infant is further stable and thereafter the volume of feeds can be increased by 10-20 mL/kg/d until full feeding volume is reached at 140 mL/kg/d to 150 mL/kg/d. Once full enteral feeding volume is tolerated hypercaloric feeds should be instituted and carefully watched for tolerance to optimize growth. In all cases, gastric residuals, their quality (undigested Vs partially digested, mucus or nutritional entity, volume, frequency), serum glucose level, signs of abdominal distension, diarrhea, blood in stool etc should be closely monitored. Serum electrolyte levels, serum glucose level, total and differential blood counts including platelets, and symptomatology of possible infection should also be evaluated. In cases of feeding intolerance or appearance of any of the above mentioned complications, feeding should be held or stopped immediately. Signs of possible NEC should be clinically as well as radiologically, biochemically and hematologically assessed in all such cases.

Breast milk is the preferred feeding. If premature formula is used, it may be diluted to ½-1/4 strength with sterile water or a glucose electrolyte solution like pedialyte, as indicated by the serum electrolyte levels, during the first few hours or days of initiation of feeding. If the diluted formula feeding is tolerated the strength can be increased to full in steps during the first 2-5 days of enteral nutrition along with the volume, as tolerated. In all these cases serum electrolyte levels should be closely monitored.

## SUMMARY

As the GI tract of VLBW infants is immature at birth it is incapable of performing full-scale digestion and absorption and is susceptible to NEC. During first 48 hours of life parenteral fluid is preferred over enteral nutrition in sick and unstable VLBW infants and these infants are given nothing enterally. However in relatively stable VLBW infants weighing < 1000 g at birth gut priming feeding can be started at a rate of < 10 ml/kg/d and closely monitored for intolerance or NEC. In VLBW infants > 1000 g who have minimal or no lung disease, are not infected and are otherwise stable, enteral feeding can be initiated as a supplement to parenteral fluid at a rate of 10-20 ml/kg/d during the first 0-48 hours of life. Thereafter enteral nutrition can be increased gradually at the same rate and closely watched for signs and symptoms of intolerance and/or NEC. Breast milk is preferred and can be used in all these cases.

## REFERENCES

1. Troche B, Harvey-Wilkes K, Engle WD, Nielsen HC, et al., Early minimal feeding promotes growth in critically ill premature infants. *Biol Neonate*, 1995. 67(3): 172-81

2. Dunn L, Hulman S, Weiner J, Kliegman R. Beneficial effects of early hypocaloric enteral feeding on neonatal gastrointestinal function: preliminary report of a randomized trial. *J Pediatr*, 1988. 112(4):622-9.
3. Kennedy KA, Tyson JE, Chamnanvanikij S. Early versus delayed initiation of progressive enteral feedings for parenterally fed low birth weight or preterm infants. *Cochrane Database Syst Rev*. 2000;(2):CD001970.
4. McClure RJ, Newell SJ. Randomized controlled study of clinical outcome following trophic feeding. *Arch Dis Child Fetal Neonatal Ed*, 2000. 82:F29-33.
5. Anderson DM, Kliegman RM. The relationship of neonatal alimentation practices to the occurrence of endemic necrotizing enterocolitis. *Am J Perinatol*, 1991. 8:62-7.
6. Rayyis SF, Ambalavanan N, Wright L, et al., Randomized trial of "slow" versus "fast" feed advancements on the incidence of necrotizing enterocolitis in very low birth weight infants. *J Pediatr*, 1999. 134:293-7.
7. Ziegler EE et al., Aggressive nutrition of the very low birth weights infant. *Clin Perinatol*, 2002. 29(2):225-244
8. Slagle TA, Gross SJ. Effect of early low-volume enteral substrate on subsequent feeding tolerance in very low birth weight infants. *J Pediatr*, 1988. 113(3):526-31.
9. Berseth CL, Bisquera JA, Paje VU. Prolonging small feeding volumes early in life decreases the incidence of necrotizing enterocolitis in very low birth weight infants. *Pediatrics*, 2003. 111(3):529-34.
10. Brown EG, Sweet AY. Preventing necrotizing enterocolitis in neonates. *JAMA*, 1978. 240:2452-4.
11. Pereira G. nutritional care of the extremely premature infant. *Clin Perinatol*, 1995. 22(1):61-75
12. Baumgart S, Costarino AT. Water and electrolyte metabolism of the micropremie. *Clin perinatol*, 2000. 27(1):131-146
13. Thureen PJ, Hay WW. Intravenous nutrition and postnatal growth of the micropremie. *Clin perinatol*, 2000. 27(1); 197-219

