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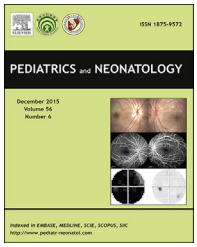

REVIEW ARTICLE

Trend of Nutritional Support in Preterm Infants

Man-Yau Ho [a], **Yu-Hsuan Yen** [b,*]

[a] *Department of Pediatrics, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan*
[b] *Department of Pharmacy, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan*

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Without appropriate nutritional support, preterm infants fail to grow after birth and have malnutrition. The main reason for delayed feeding is fear of immaturity of gastrointestinal function. The principles of nutritional practice should be as follows: (1) minimal early initiation of enteral feeding with breast milk (0.5–1 mL/h) to start on Day 1 if possible and gradual increase as tolerated; (2) early aggressive parenteral nutrition as soon as possible; (3) provision of lipids at rates that will meet the additional energy needs of about 2–3 g/kg/d; and (4) attempt to increase enteral feeding rather than parenteral nutrition.

1. Problems of nutrition in ill preterm infants

Most preterm neonates fail to grow after birth, and they are often affected by respiratory distress and immaturity. Malnutrition may occur without appropriate nutritional support.[1] Preterm infants do not usually fully catch up to normal rates of growth, and it takes a mean of 14–17 days to regain birth weight in infants of <1000 g at birth.[2,3] Very-low-birth-weight infants are characterized by significant weight loss in the initial days and weeks because of catabolic illness and insufficient protein energy supply.[4] The most common reason is that mechanical ventilation and high oxygen concentrations cause pulmonary and systemic inflammatory processes.[5] In the traditional nutrition model, for preterm neonates with respiratory distress syndrome, enteral nutrition and parenteral nutrition (PN) were often delayed. The reasons for the preterm neonates to have delayed feeding are fear of (1) respiratory distress syndrome and mechanical ventilation, (2) immaturity of gastrointestinal function, (3) systemic hypoxia, (4) catabolic stage, and (5) necrotizing enterocolitis (NEC; Table 1). Consequently, enteral feeding may be delayed for several days, partly because of gastrointestinal immaturity to digest and absorb the complex nutrients in preterm neonates.[6,7] Often, intravenous (IV) amino acids are not given immediately after birth, and when provided they are

* Corresponding author. Department of Pharmacy, Wan Fang Hospital, Taipei Medical University, Number 111, Hsing Long Road, Section 3, Taipei 116, Taiwan.
E-mail address: sandrayen@tmu.edu.tw (Y.-H. Yen).

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Table 1 Frequent reasons for delayed feeding of preterm infants.

Type of delayed feeding	Reason for delayed feeding	Source of fear
Enteral feeding	Abdominal distension	NEC
	GER	Apnea
	Hyperglycemia &/or rebound hypoglycemia	Poor metabolism & infections
	Low SPO_2	Slow metabolism of nutrients
	On CPAP	Air entering the stomach
	On ventilator	Slow digestion & absorption
Parenteral nutrition	UA &/or UV catheters	Gut ischemia & NEC
	High BUN	Urea & amino acid toxicity
	Hypo or hyperkalemia	Interfere with poor gut function
Lipid emulsion	High bilirubin	Interfere with bilirubin binding
	Hyperlipidemia	Accumulation in reticuloendothelial system & in lungs

BUN = blood urea nitrogen; CPAP = continuous positive airway pressure; GER = gastroesophageal reflux; NEC = necrotizing enterocolitis; SPO_2 = saturation of peripheral oxygen; UA = umbilical artery; UV = umbilical vein.
Note. From "Aggressive nutrition of the very low birthweight infant," by E.E. Ziegler, P.J. Thureen, and S.J. Carlson, 2002, *Clin Perinatol*, *29*, p. 225—44. Copyright 2002, Elsevier Inc. Reproduced with permission.

given in low amounts. The dose of IV amino acids is usually <3 g/kg/d, and then it is increased slowly, taking several days to reach an appropriate amount.

2. Early initiation and gradual advancement of enteral feeding

How early should enteral feeding be given? Should it commerce within the first 24 hours or 48 hours? Early feeding within the first 24 hours after birth can induce the release of trophic endogenous agents and inhibit the effects of inflammatory mediators and cytokines released in critically ill children.[8,9] The first option is early minimal enteral feeding after birth, namely, trophic or priming feeding. Early and gradual advancement of enteral feeding can promote release of gastrin and then full breast-feeding can be achieved.[10] Early feeding can help develop intestinal villi and activate enzymes, improving digestion, absorption, and motility. Early feeding can also help develop gut microbiota, thereby preventing infection and NEC, and it can also help reduce local and systemic inflammation.[11,12] Human milk is preferred in feeding, particularly for preterm and sick infants. If the mother's breast milk is insufficient, donor breast milk from the milk bank may be used. Preterm infants should receive breast milk as soon as possible after birth. Breast milk consumption can stimulate the release of endocrine and metabolic factors such as gastrin, enteroglucagon, motilin, neurotensin, gastroinhibiting peptide, and pancreatic polypeptide. Using breast milk with the growth of Bifidobacteriae and *Lactobacillus* strains can help gastrointestinal absorption and motility.[13] The fat content of breast milk is important to infant development when it comes to the omega-3 fatty acid docosahexaenoic acid, and the omega-6 fatty acid metabolite arachidonic acid, which are both concentrated in the infant brain during the last trimester and in the 1st year of life.[14] The omega-3 fatty acid is alpha-linoleic acid from the production of essential long-chain polyunsaturated fatty acids, docosahexaenoic acids, and arachidonic acids. Omega-3 fatty acids play an important role in retinal and neurologic development.[15] The use of human milk fortifier (HMF) helps to meet the high nutritional requirements of the human milk-fed premature infant.[16] Some studies have shown that the addition of HMF is associated with short-term improvements in weight, height, bone mineralization, neurologic outcome, and head growth.[17—21] However, HMF showed an increase in osmolarity of breast milk.[22] Some studies showed that the addition of HMF temporarily delayed gastric emptying and caused a short-term increase in gastric residuals and emesis.[21,23—25] Another study showed increased infections and NEC in infants who were fed fortifier versus nonfortifier human milk.[26]

The American Society for Parenteral and Enteral Nutrition suggested in 2009 that extremely-low-birth-weight and very-low-birth-weight infants might benefit from minimal enteral feeding, stating very slowly at 0.5—1 mL/kg/d and increasing to 20 mL/kg/d.[27] Feeding volumes are to be kept low regardless of the size of gastric residuals, and are then gradually increased when gastric emptying is improved.[28] In summary, small amounts of enteral feeding through nasogastric tube to supplement PN are given as early as the 1st day of life at birth in preterm infants.

3. Early aggressive PN

In the past 20 years, the practice in PN is to gradually increase the amount of amino acid intake and to shorten the time after birth to start parenteral alimentation.[29] A preterm neonate without a supply of protein may have an endogenous protein loss of 0.5—1.0 g/kg/d.[30] Giving amino acids during the first hours of life with a goal of reaching fetal nutrient delivery rates as soon as possible is a cornerstone of this strategy. This strategy is the key to avoid the period of early neonatal malnutrition. Plasma amino acids fall within hours although hepatic enzyme activity is low.[30] Amino acids are important in the synthesis of insulin, insulin-like factors, and other growth-related hormones.[31,32] Earlier undernutrition can reduce the production of serum insulin-like growth factor-1. Low serum

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