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Review Article

Postnatal Nutrition during the Early Stage after Extremely Preterm Infants Born

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Abstract

Optimizing nutrition in extremely preterm (EPT) infants has been a major strategy to improve the quality of neonatal intensive care. However, there is no standard for accurately assessing the nutritional status of preterm infants, nor is there a clear consensus on the actual nutritional practices. Careful management of nutrients intake is essential to optimize outcomes for EPT infants. It is clear that just a few weeks of insufficient nutrition can lead to permanent disadvantage. Appropriate nutritional management before discharge may prevent the occurrence of nutritional deficit at discharge or continuously.

Keywords: *Extremely Preterm (EPT); Postnatal Nutrition; Extremely Preterm Infants*

Achieving normal growth is currently the biggest clinical challenge for extremely preterm (EPT) infants. There are significant physiological and metabolic differences between preterm infant and fetus, so the criteria for intrauterine growth may not be entirely appropriate [1]. Understanding of precise energy and protein requirements in ELBW infants and providing them with nutritional support after birth will change their nutritional outcomes.

Nutrients requirements in extremely preterm infants

Body stores of a weighing 1000g infant can only provide sufficient energy for 4 - 5 days [2]. Factors such as the limited ability of preterm infants to metabolize nutrients, fluid restriction by neonatologists to reduce patent ductus arteriosus or chronic lung disease, intrauterine growth retardation in some infants before birth, and increased energy expenditure due to severe illness in most EPT infants, make postnatal growth retardation inevitable [3]. Careful management of energy and protein intake is essential to optimize outcomes for EPT infants because these infants are nutritionally vulnerable. However, the nutritional requirements of EPT infants remain uncertain due to limited data.

Studies [4-6] have shown that no dietary protein intake in the first week after birth will lead to a negative nitrogen balance of about 150 mg/kg/d, which is equivalent to 0.9 - 1.0 g/kg/d protein. It suggests that infants born at 25 - 30 weeks require 3.5 - 4.0 g/kg/d of protein intake [7]. 1 g/kg protein intake per day is necessary to maintain zero nitrogen balance. Over 1 g/kg/d of protein is needed to achieve positive nitrogen balance, and EPT infants are likely to need more protein.

Both glycogen and fat stores are limited in EPT infants. Increasing protein and energy intake through enteral feeding during the first few days of life leads to an inevitable nutritional deficit. Embleton., *et al*. [8] found that infants born less than 31 weeks gestation have a total protein deficit of < 8 g/kg/d and an energy deficit of < 600 kcal/kg at the end of the second week of life. These cumulative deficits are based on the assumption of 120 kcal/kg/d energy and 3 g/kg/d protein. EPT infants are prone to malnutrition without obvious signs. Additional daily replenishment requires to catch up depends on the time of deficit recovery.

For infants without fat malabsorption but with growth retardation, increasing their energy intake may not be appropriate as other nutrients (especially protein) are more likely to limit growth [9]. Short-term data suggest that EPT infants require more than 3 g/kg/d of protein, but there are too few data to know what the optimal protein intake is for most EPT infants.

Nutritional support in early stage after extremely preterm infants born

One of the goals of the NICU team is to provide nutrition to the EPT infants to achieve a similar growth velocity (GV) as in utero [10]. Actually, the GV of extremely low gestational age infants often does not reach the GV of intrauterine fetus in late pregnancy, and this growth deficit leads to extrauterine growth restriction in a large proportion of infants, which lasts until early childhood [11,12].

Parenteral and enteral nutrition given to EPT infants during the early postnatal period (within 24 hours) results in rapid weight recovery, improved weight gain, and earlier achievement of full enteral feeding [13]. Martin., *et al*. [14] provided nutritional support (parental nutrition and enteral feeding) to 1187 extremely low birth weight (ELBW) infants after birth at 14 institutions and calculated (GV) between days 7 and 28. The protein and fat intake in nutritional practice was close to the nutritional recommendations at that time, while the carbohydrates and total energy intake were not in this population. GV of the infants exceeded the guideline of 15 g/kg/d. However, they found that 75% of infants had extrauterine growth restriction by 28 days, compared with 18% at birth. A GV of 20 - 30 g/kg/d was associated with ELBW infants' maintaining or exceeding their birth weight Z score. Nutritional practices in the early postnatal period (day 7) were positively correlated with GV calculated between days 7 - 28. Early nutrition delivery is an important factor in postnatal growth. The incidence of extrauterine growth retardation remains high in ELBW infants even when they achieve GV as recommended by current guidelines.

The fetus receives nutrients from the placenta, and when an EPT infant is born, it is in urgent need of nutritional supplements. Parenteral nutrition support various nutrients to the EPT infants in the early stage of birth until enteral feeding is established [15]. Previous studies have shown that parenteral nutrition administrated immediately after birth is associated with postnatal weight loss and shortened time to regain birth weight [16]. Higher energy and protein intake was associated with less decline in weight standard deviation score (WSDS) from birth to 28 and 70 days of age [17]. Although evidence support an association between early amino acid intake and weight gain and neurodevelopment in EPT infants, the discrepancy between NICU practice and recommendation is a barrier to adequate amino acid administration in early postnatal life of EPT infants born [18-20]. Amino acids has always been a hot spot in neonatal nutrition research, but it is also important to provide adequate glucose and energy in the early postnatal period. Glucose is an important source of energy for the brain and vital organs of newborns. Early lipid emulsion delivery is associated with long-term neurological development in EPT infants. Lipid emulsions should be administered not only to match metabolic demands of EPT infants but also to prevent essential fatty acid deficiency. The optimal dosage, timing of use, and product selection of lipid emulsion for EPT infants should be determined by more high quality research [21].

Enteral feeding is the key to promote gastrointestinal tract development, and inappropriate feeding methods can hinder the growth of intestinal mucosa. The occurrence of NEC is one of the main problems hindering enteral feeding. Jadcherla., *et al*. [22] used SIMPLE feeding strategy to make premature infants achieve full enteral feeding faster, reduce the incidence of NEC, and promote improvement of neurological development. Breast milk is the first choice for feeding EPT infants. However, some nutrients in breast milk, such as calcium, phosphorus and protein, cannot meet the needs of EPT infants, so human milk fortifier is needed to improve growth.

Early nutritional intakes and substantial neonatal morbidity in EPT infants

In EPT infants, bronchopulmonary dysplasia (BPD) and retinopathy of prematurity (ROP) are common diseases during hospitalization, which are related to developmental impairment of the lungs and retina [23,24]. Poor growth in EPT infants is associated with the incidence of BPD and severe ROP (grade ≥ 3), which are also associated with morbidity risk in adulthood, including neurocognitive impairment [25].

A case-control study to investigate the relationship between nutritional intake in the first month of life and BPD development in extremely preterm infants was reported by Malikiwi group [26]. A low 4-week averaged daily energy intake was one of independent predictors for BPD development. Those BPD infants suffered feed intolerance and enteral feeding delay due to their lower gestational age and birthweight, impact of PDA on gut perfusion and lower caloric-to-volume ratio. Another study, a population-based study [27] including 498 extremely preterm infants born before 27 gestational weeks, classified according to the stage of ROP. It showed that low energy intake was an independent risk factor for severe ROP during the first 4 weeks after born, and adequate energy (from PN and enteral feeding) may reduce the risk of severe ROP in extremely preterm infants. Klevebro., *et al*. [28] administered nutritional intervention to 296 infants with a median gestational age of 25 3/7 weeks. In infants mechanically ventilated for less than 10 days, weight standard deviation score (WSDS) at day 7 increased by 0.08 (95% CI 0.06 - 0.11, P < 0.001) for each 10 kcal/kg/d increase in energy during days 4 - 6; For each 10 kcal/kg/d increase in energy intake between days 7 and 27, the risk of BPD was reduced by 9% (95% CI 1 - 16, P = 0.029) and the risk of ROP at any level was reduced by 6% (95% CI 2 - 9, P = 0.05). Infants with mechanical ventilation for more than 10 days need higher energy and protein intake to reduce the risk of BPD. Their findings suggest the importance of energy and protein intake in EPT infants with critical illness.

Summary

Optimizing the nutrition of ELBW infants is one of the main strategies to improve the quality of NICU. It is clear that just a few weeks of insufficient nutrition can lead to permanent disadvantage. Inadequate nutrition intake may be a risk factor for major complications in ELBW infants and, in turn, a higher burden of disease is a risk for growth restriction. Reasonable nutritional management before discharge may prevent the occurrence of nutritional deficit at discharge or continuously. However, there is no standard for accurately assessing the nutritional status of preterm infants, nor is there a clear consensus on the actual nutritional practices. The optimal nutritional support, including parenteral and enteral nutrition for ELBW infants should be determined by more high quality research.

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