High-Protein Formulas

Evidence for Use in Preterm Infants

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KEYWORDS

• Preterm • Prematurity • Enteral feeding • Formulas • Preterm formulas
• Premature infant formulas • High-protein formulas • Protein

KEY POINTS

- Growth rates and body composition of very low birth weight preterm infants (<30 weeks' gestation, <1500 g birth weight) require 3.5 to 4.5 g/kg/d of protein in enteral formulas (or milks, mother's own or donor) at usual feeding rates (150 mL/kg/d); but the requirement for protein decreases as gestational age and birth weight advance towards term and growth rates decrease.
- Both energy and protein are required in formulas to promote growth and development, though recent studies indicate that if the protein/energy ratio in formula is too low it can promote excess fat deposition in adipose tissue that may lead to later-life obesity and associated complications.
- Deficiencies in brain, heart, lungs, liver, pancreas, kidney, and skeletal muscle have been found following preterm birth and the usual undernutrition that preterm infants receive; such deficiencies can last for the lifetime of the affected infant.
- Tables included in this article document formulas that are enriched in protein for preterm infants.

NUTRITIONAL GOALS FOR PRETERM INFANTS AND THE NEED FOR NUTRIENT-ENRICHED FORMULAS

The generally accepted goal for nutrition of the preterm infant is to achieve and maintain the growth rate and body composition of the normally growing, healthy human fetus of the same gestational age.[1] Recent efforts to meet this goal include the administration of intravenous nutrition earlier after birth and at higher rates than previously used and supplements to breast milk (mothers' own milk and donor milk); these efforts

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are discussed elsewhere in this edition of *Clinics in Perinatology* by Stephens and Vohr in their article about protein intake and neurodevelopmental outcomes, as well as Adamkin and Radmacher in their article about the fortification of human milk for very low birth weight infants. Human milk supplemented with bovine milk–derived or human milk–derived fortifiers is the preferred enteral feeding of choice for preterm infants because of its protective effects against infection and necrotizing enterocolitis.[2–4] A mainstay of nutrition for preterm infants over the past 30 to 40 years, however, has been the use of preterm formulas or formulas designed to meet the additional protein, energy, and micronutrient requirements of the preterm infant. Preterm formulas contain more protein (2.4 g/100 mL or 3 g/100 kcal), energy (67.6–101.0 kcal/100 mL), calcium (133–146 mg/100 mL or 165–180 mg/100 kcal), and phosphorus (67–81 mg/100 mL or 83–100 mg/100 kcal) than standard formulas for term infants. New generations of high-protein preterm formulas are now available that contain even higher protein contents (2.68–2.9 g/100 mL or 3.3–3.6 g/100 kcal). Essentially all studies have documented that inadequate nutrient intakes in preterm infants have resulted in widespread postnatal growth restriction.[5,6] As a result of inadequate postnatal nutrition, infants are at risk for long-term growth and neurodevelopmental impairment.[7–11] Adequate protein intake, similar to what the fetus would receive in utero, is essential for the preterm infant to maintain growth, body composition, and nitrogen balance.

COMPLICATIONS OF INSUFFICIENT PROTEIN DELIVERY TO PRETERM INFANTS

The use of fortified human milk and/or preterm formula has resulted in greater success at achieving increased growth in weight, length, and head circumference at hospital discharge and close-to-term gestational age.[12] Such improved growth also has translated into improved, longer-term neurodevelopmental outcomes.[13–15] Nevertheless, preterm infants develop body compositions by term-corrected gestational age that are characterized by lower lean mass (LM) and relatively increased adiposity (particularly in intra-abdominal regions) in comparison with normally growing human fetuses.[16,17] Furthermore, very low birth weight (VLBW, defined as birth weight <1500 g) preterm infants experience marked linear growth suppression (stunting) that continues at least 2 years beyond hospital discharge and contributes to shorter stature even into adolescence and early adulthood.[18] A principal reason for such continued growth delays is that nutrition remains inadequate, especially in the first 2 to 4 weeks of life when physiologic instability precludes consistent protein and energy delivery.[19,20] Even when aggressive nutritional approaches are used, deficits in protein and energy still accumulate during the hospital stay of a preterm infant.[21] In addition, providing an optimal ratio of protein/energy (P/E) that fuels normal body composition is critical. If energy content of the formula is in excess relative to protein, whole-body growth can favor fat deposition over LM. On the other hand, if protein is in excess relative to energy, the excess protein may be catabolized for energy rather than to support LM growth.

Weight, length, and occipitofrontal head circumference measurements are the mainstays of monitoring growth in the neonatal intensive care unit (NICU). They are used to represent the growth and development of essentially all of the body organs in preterm infants, including the brain.[22] These measurements are positively associated with neurodevelopmental outcomes in preterm infants.[8,17,23] Conversely, poor linear growth has been implicated in worse neurodevelopmental outcomes.[11] Indeed, several studies have shown that improved nutrition with higher amounts of protein and energy intake in the postnatal period in the preterm infant correlates with increased length and head circumference at term-corrected gestational age[24–26] and with