Premature Infant Nutrition: Exploring the Ratio of Protein to Nonprotein Calories

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Background: Very low birth weight (VLBW, <1500g) infants historically received high rates of intravenous glucose and lipids. These infants developed increased fat deposition; however, growth of head circumference and length, factors which require protein intake, remain restricted. Although protein intake is recognized as an important factor, optimal growth is not achieved solely through high protein nutrition. A positive nitrogen balance is required to achieve an anabolic state of protein synthesis; therefore, growth requires both protein and non-protein energy. There is a delicate balance between protein and non-protein energy in order to promote growth and limit deleterious effects, measured as the protein to non-protein calorie (P:NPC) ratio. This ratio is not routinely evaluated in the clinical management of the preterm infant.

Objective: To describe the P:NPC ratio in VLBW infants. To determine the magnitude of association with caloric intake, and whether the ratio is associated with parenteral nutrition or disease status.

Study Design: A retrospective analysis of 115 VLBW infants admitted to a level 4 neonatal intensive care unit between 2011 and 2014. Daily nutrition intake and details of enteral and parenteral nutrition were collected for each patient through the first 42 days of life. Distributions of P:NPC ratios were calculated. This data was subsequently used to analyze bivariable associations between the ratio (g/100kcal) and total calories (kcal/kg), receipt of parenteral nutrition, and presence of comorbid conditions including patent ductus arteriosus (PDA), necrotizing enterocolitis or spontaneous intestinal perforation (NEC/SIP), small for gestational age and intubation at day 28 of life. Variables found to be significant in the bivariable analysis were subsequently used in a multivariable analysis to adjust for confounding factors. Mixed effects linear regression was used to perform all analyses to account for repeated measures from each patient.

Results: The median P:NPC ratio for 115 infants was found to be 4.1 g/100kcal (range 0-16.6 g/100kcal). The P:NPC ratio was found to be independently associated with total non-protein calorie intake (-0.5 g/100kcal for every 10kcal/kg; $P<0.001$) and parenteral nutrition (0.2 g/100kcal; $P<0.001$). Comorbidities including PDA, NEC/SIP, and intubation at day of life 28 were not associated after adjusting for total non-protein calorie intake and phase of nutrition.

Conclusion: VLBW infants received P:NPC ratios above goal. This study identifies two areas to focus on to improve clinical nutrition. First, the association between the ratio and total non-protein calorie intake suggests that the elevated ratio is related to a decrease in caloric intake. Second, there is also a clinically meaningful association with parenteral nutrition. As infants transition from parenteral to enteral nutrition, the complexity of nutrition delivery decreases. Parenteral nutrition requiring human calculations is replaced with breast milk or formula with standard P:NPC ratios. The P:NPC ratio is not a commonly discussed topic, especially in a clinical setting. Whether the P:NPC ratio is a clinically useful tool for optimizing growth and minimizing negative effects warrants further attention.