Protein in Neonatal Nutrition: Not Too Little Not Too Much

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Protein in Neonatal Nutrition: Not Too Little Not Too Much

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Preterm Infants: How Safe are High Protein Intakes?

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Term Infants: How Much Protein is Too Much?

Ferdinand Haschke, Austria
Preterm Infants: How Safe Are High Protein Intakes?

Prof. Hans van Goudoever
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Abstract

Postnatal growth failure is widespread among small premature infants\(^1\).

Growth failure is linked to cognitive impairment in a dose-dependent fashion\(^2,3\). Protein is considered the driving force of growth for (preterm) infants, when energy supply is in surplus\(^4\). To prevent growth failure, recommendations from pediatric societies around the world showed a gradual increase in amount of protein over years\(^5,6\). Not only for enterally fed, also for parenterally fed infants, amino acid recommendations also showed an increase in amounts, and, as importantly, a reduction in time to withhold amino acid administration following birth. The use of modern techniques to improve the quality has led to a more widespread and direct use of these mixtures\(^7\).

However, long term effects of this change of policy are lacking, although some recent reports have provided us with some data. In a two years follow-up study of a higher parenteral amino acid intake, no clear benefits were shown\(^8\). Another recent study did not show either a beneficial effect of providing an additional gram of amino acids/protein throughout the NICU stay\(^9\), although others did find an effect of cumulative protein
intake on neurodevelopmental outcome\textsuperscript{10}. Higher protein intakes during the post-discharge period does not seem to influence neurocognition at age 8 years\textsuperscript{11}.

The largest multicenter, randomized, controlled trial involving 1440 critically ill children to investigate whether withholding parenteral nutrition for 1 week (i.e., providing late parenteral nutrition) in the pediatric intensive care unit (ICU) was clinically superior to providing early parenteral nutrition revealed that the rate of patients with new infections was increased as was the duration of the intensive care stay\textsuperscript{12}. Especially neonates were at risk\textsuperscript{13}. Secondary analysis revealed that amino acids were causing the harm, not so much the lipids or glucose\textsuperscript{14}, possibly due to a disturbed autophagy process\textsuperscript{15,16}. Importantly, two years after PICU admission, not providing supplemental PN early in PICUs did not negatively affect mortality, growth or health status, and significantly improved neurocognitive development\textsuperscript{(17)}. No preterm infants were included in this trial so it remains the question whether these findings can be extrapolated to the NICU population who are frequently less sick than term infants at the PICU. But surely we need a well designed trial to investigate whether provision of high amounts of amino acids/proteins in early life are safe, and beneficial for premature infants.
References:


Term Infants: How Much Protein Is Too Much?

Prof. Ferdinand Haschke
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Abstract

What is known:

Nutrition during the first 1000 days of life (i.e. from conception to 2 years) has a long-term effect on health and metabolic outcome.

Preterm infants have high protein needs but in clinical practice it is often difficult to meet those high requirements, in particular when preterm infants are fed fortified human milk and during the early post-discharge period. Term infants have lower protein requirements than previously estimated and those who were fed formulas during the past decades received much more protein than breastfed infants. High protein intake can be associated with rapid weight gain during the first 12 months and increased risk of obesity during childhood, adolescence, and adulthood. Disturbed metabolic outcome and higher diabetes- and cardiovascular disease risks could be long-term adverse effects.
Evidence from clinical studies:

There is growing evidence that low protein intake with breast milk during infancy and early childhood can help to protect from accelerated weight gain and childhood obesity: already 2-3 decades ago, studies compared weight, length, and weight for length ratios of infants who were breastfed or fed old high-protein infant formulas. Those studies indicated that breastfed infants were leaner at 2 years. Protein intake of breastfed infants was almost 50% lower and their blood levels of branched chain amino acids, insulin-, and IGF1 levels were lower as well. Longitudinal cohort studies with large sample sizes that reflect the Dutch- and French childhood populations now confirm that higher protein intake during the first 24 months is associated with higher BMI during school age, adolescence, and young adulthood. Results of RCTs that compared and followed-up growth, metabolic outcome and body composition of term infants who were fed (0-12mo) high- or low-protein formulas (+ breastfed reference groups) are available now. They indicate lower weight, weight-gain, and fat mass until 2 years in the breastfed- and low protein formula groups than in the high protein formula groups\textsuperscript{1,2,3}. Follow-up of
the RCTs until 2-6 years indicates lower BMI, subcutaneous fat, % body fat, and lower obesity prevalence in the breastfed- and low protein formula groups. A recent study from New Zealand (RCT) shows that lower protein intake between 12-24 months might also be beneficial: % body fat and absolute fat mass at 2 years were lower in a cohort of toddlers who were fed a low-protein young child formula (growing-up milk) when compared to a group who received cow’s milk). Health economic data suggest lower risk of obesity related diseases later in life (diabetes, myocardial infarction, stroke) if infants are breastfed or fed low protein formulas and indicate 3.9% cost savings for the population because of lower health care costs and higher productivity later in life.

Conclusions:

From RCTs there is evidence that low protein intake with breast milk or with high quality low-protein formulas can contribute to prevention of later obesity.

The effect size has been estimated to be as high as 20%. Therefore, promotion of breastfeeding beyond 6 months should be our goal. Recently an international scientific committee confirms that a high-quality low protein formula is effective to prevent from later obesity, if infants cannot be breastfed or when the breastfeeding period is shorter than recommended. The European-(EFSA) and American(FDA) food regulatory agencies confirm that high quality low-protein formulas are safe.
References:

1. Haschke F et al: Nutritive and Bioactive Proteins in Breastmilk
   Ann Nutr Metab 2016;69(suppl 2):126
   at school age: follow-up of a randomized trial. Am J Clin Nutr 2014;99:1041-1051
3. Alexander et al: Growth of infants consuming whey-predominant term infant
   formulas with a protein content of 1.8 g/100 kcal: a multicenter pooled analysis
   of individual participant data. Am J Clin Nutr 2016;104;1083-1092
4. Wall CR et al: A multicenter, double-blind, randomized, placebo-controlled trial
   to evaluate the effect of consuming Growing Up Milk “Lite” on body composition
5. Marsh Ket al: The Economic Impact of Lower Protein Infant Formula for the
   Childhood and its Implications for Maternal and Long-Term Child Health:
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