Amino Acid Homeostasis in the Preterm Infant

Johannes B. van Goudoever

Observational studies have suggested that inadequate nutrient intakes in the first few days to weeks following birth have adverse effects on long-term neurocognitive function [1–3]. Unfortunately, only a few prospective studies have been conducted. These studies, most originating in the 1980s, have shown that both quantity and quality of the provided nutrients to preterm children and subsequent growth have pronounced effects on neurocognitive function [4], cardiovascular health [5, 6] and metabolic status [7, 8]. These effects seem to persist over a long period, well beyond childhood [9, 10].

Undernutrition, with subsequent growth failure, occurs predominantly in the first week of life of premature infants. Recent recommendations for enteral nutrition prevent undernutrition during the enteral phase [11, 12]. However, many neonatologists are reluctant to start with high nutrient intakes directly following birth. They fear that the renal and hepatic system are not developed enough to handle high amounts of parenteral administered nutrients and their metabolites. That seems logical since in utero, the placenta and the mother have large capacities to handle possible detrimental metabolites. Present amino acid mixtures and lipid emulsions are improved when compared to mixtures that were marketed years ago. However, providing high amounts of nutrients form birth onwards should be carefully evaluated, and randomized trials with ample power should be conducted. Not only short-term proxy outcome variables should be measured, but also long-term follow-up should be included as end points of such trials.

We have recently performed two trials, where we investigated the effects of only very small changes in our direct postpartum nutritional management. In our first randomized controlled trial, we aimed to find a difference in nitrogen balance, a proxy for anabolism, on day 2 of life by supplying 2.4 g of amino acids per kilogram per day from birth, whereas the control group received dextrose only [13]. The latter group started after 36 h with 1.2 g of amino acids, with an increase to 2.4 g on
day 3 of life. Despite very low energy intakes (30–50 kcal/kg per day), the preterm infants with an average birthweight of 1 kg were able to use the provided amino acids; whole-body protein synthesis [14] and albumin synthesis [15] increased, and nitrogen balance turned from negative (catabolic state) to positive (anabolic state) [13]. In addition, the synthesis rate of the main intracellular antioxidant glutathione was higher as well [16]. We could not detect any negative side effects. So, this study showed that supplementing preterm infants with 2.4 g amino acids per kg per day resulted in a clear beneficial effect in the short term. Others questioned the efficiency and warned about possible detrimental effects [17, 18]. Very recently, long-term follow-up from one of these studies became available, showing diminished growth during the first 2 years of life in a small group of infants (n = 43) [19]. Cumulative and single plasma AA concentrations negatively correlated with Mental Developmental Index and postnatal growth.

Two-year follow-up of our own trial (follow-up n = 111, 98% of those eligible) revealed no detrimental effects. Even to the contrary, preterm boys were significantly more alive without major handicaps if they were supplemented with high amino acid intakes from birth onwards. No significant effect was noticed in girls [submitted]. Very recently, we finished our second trial on early nutritional support of small infants. 144 infants were included, with different lipid and amino acid intakes from birth onwards. The highest intake group (3.6 g amino acids and 2 g lipids) was most anabolic, as shown by stable isotope techniques and classic nitrogen balances.

In conclusion, optimal nutritional strategies for preterm infants are still being developed. Long-term consequences of quality and quantity of nutrients are likely to be established, even during the first few days of life. Long-term follow-up of interventions should be obligatory to evaluate the choices made in feeding this vulnerable population.

References


