How Proteins Improve the Development of Preterm Infants

W.E. Corpeleijn, C.H. van den Akker, J.A. Roelants and J.B. van Goudoever

Amino acids and proteins play a pivotal role during growth and development. Besides acting as building blocks during tissue synthesis, amino acids or proteins act specifically by upregulating defense systems or by stimulating key sites in metabolic pathways. After premature birth, the neonatologist is responsible for delivering the right amount and quality of nutrients to the neonate. It is increasingly recognized that amino acids in the immediate postnatal phase have both short- and long-term influence on the developing infant. In the short term, undernutrition or malnutrition can result in increased vulnerability to infectious diseases [1], higher susceptibility to lung injury caused by impaired tissue repair and muscle weakness [2], and decreased maturation of the intestine [3–4] or brain [5]. The causes of inadequate nutrient intake include fear of intolerance of parenteral and enteral nutrition. Also, fluid intake is restricted to minimize complications such as patent ductus arteriosus and chronic lung disease. Third, acute neonatal illness such as sepsis and necrotizing enterocolitis as well as metabolic derangements such as hypertriacylglycerolemia or severe uremia all result in a reduced nutrient administration.

After premature birth, the intestine is not capable of tolerating the large amounts of substrates that are mandatory to ensure optimal development. Therefore, sufficient amounts of amino acids, in combination with the appropriate amount of energy, should be administered to the infants by the parenteral route. Amino acid administration from birth onwards has been proven to be well tolerated by preterm infants. It reverses a negative nitrogen balance towards anabolism, and it increases plasma amino acid concentrations towards reference ranges found in fetuses or healthy neonates [6–8]. Possible involved pathways, other than providing anabolism, include reduction of oxidative stress by upregulating glutathione synthesis rates [9]. In addition, the increased synthesis rate of e.g. albumin following amino acid
administration, may be responsible for an increased transport and binding capacity, with a reduction of potentially toxic levels of free bilirubin or medicines [10]. Stephens et al. [11] found that in extremely low-birthweight infants, after adjusting for confounding variables related to disease, an increase of 1 g/kg per day of protein intake during the first week of life was associated with an 8.2-point increase in mental developmental index at 18 months of age. Studies in infants less than 26 weeks’ gestation are however very scarce and warrant some caution if protein is administered in high doses.

Nonetheless, total parenteral nutrition itself is associated with complications like sepsis and cholestasis. Therefore, it is mandatory to bring the intestine as soon as possible to a condition that allows enteral nutrient administration in high amounts. Premature infants fed own mother’s milk are known to tolerate full enteral feeding earlier compared to their formula-fed peers [12]. Biologically active proteins present in human milk but not in formula, like IGF-I, IGF-II and EGF, are thought to stimulate maturation of the premature gut [13]. But also other human milk proteins exert a biological effect before they are digested and absorbed as amino acids. They can for example aid in nutrient absorption (e.g. bile salt-stimulated lipase) and provide protection against pathogens (e.g. immunoglobulins). Human milk generally does not contain enough protein (and energy) to meet the high demands of the very-low-birthweight infant. Therefore, multinutrient supplements composed of extra protein and carbohydrate, but also vitamins and minerals are added. By fortifying human milk in this way, however, one must note that a source of cow’s milk protein is introduced into the infant’s diet. Based on the observation that there is a higher incidence of necrotizing enterocolitis in formula-fed infants, it can be hypothesized that this is not due to protective effects of human milk but rather to a sensitizing or disrupting effect of milk (protein) derived from cows [14]. Whether a diet completely based on human milk (proteins) offers advantages over a diet partially based on cow’s milk proteins needs to be confirmed in large randomized trials.

Premature infants are born at a time which, in utero, is characterized by rapid brain and body growth. Large amounts of amino acids and other nutrients required to achieve this rapid growth are continuously supplied through the umbilicus. At birth, this nutrient supply ceases, and when the nutrient supply is not adequately restored directly after birth, the neonate slips into a malnourished state and its development is hampered. Evidence is accumulating that when an organism is malnourished during fetal or early life, it anticipates receiving a low nutrient supply in later life by adjusting the setting of hormones and metabolism. This adjusted setting makes the individual more prone to
diseases such as diabetes and metabolic syndrome in later life. Therefore, adequate nutrition in early life can be considered a preventative measure against adult-onset diseases.

References