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Editorial

The Challenge of Feeding Very Low Birth Weight Infants

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Editorial

Survival of preterm infants has markedly increased during the last decades, especially at a decreasing gestational age, due to advances in prenatal and perinatal care but prematurity continues to be a major contributing factor for neonatal morbidities and poor later auxological and neurodevelopmental outcomes [1,2].

Early nutrition plays a critical role in promoting brain development both during fetal life and the first months after birth and, as a result, the provision of adequate nutrients in the early postnatal period in preterm infants is associated with better neurocognitive outcomes [3-5]. Tan *et al.* [4] found that limiting early energy deficits by providing high energy intake, in association with increased protein intake during hospital stay, may support adequate postnatal brain growth and improve neurodevelopmental indices at 3 months of corrected age. Consistent with these findings, Stephens *et al.* [5] reported a positive, independent association between first week protein and energy intake and Mental Developmental Index Scores assessed using the Bayley Scales of Infant Development II, in extremely preterm infants at 18 months of corrected age. Better nutritional support is associated with improved growth which, in turns, is associated with better neurodevelopment outcomes [6,7]. Specifically, Ehrenkranz *et al.* [7] found that the incidence of cerebral palsy or of developmental delay fell significantly with increasing of growth velocity from birth to discharge. The positive effect of improved early growth on neurodevelopment appears to track into adulthood as reported by Sammallahti *et al.* [8]. The authors assessed a cohort of 103 adults born with a very low birth weight and reported an association between faster head circumference growth from birth to term and better general neurocognitive abilities, executive functioning, and visual memory in young adulthood.

Although it has become clear that the optimization of nutritional management of preterm infants leads to better growth, contributes to the prevention of morbidities and promotes positive neurodevelopment outcomes, the optimal nutritional management of preterm infants still represents a major challenge for neonatologists. Indeed, postnatal growth retardation, especially in the most preterm infants, remains a common finding being facilitated by nutritional practices that allow the development of severe nutrient deficiencies during the first few weeks of life [9]. Furthermore, preterm infants during hospitalization have to face several morbidities and undergo treatments that further contribute to the development of postnatal growth retardation at time of discharge [10]. As very preterm infants represent a nutritional emergency, early and aggressive nutritional management has been recommended in order to limit the degree of postnatal growth retardation [11]. With regard to energy intake, it has been estimated that 50 kcal/kg/day cover preterm infants' energy requirements for basal energy expenditure. In order to achieve growth, the provision of energy beyond these basal requirements is recommended [12]. Herrmann *et al.* [13] reported that the provision of more calories than the basal energy requirement on parenteral nutrition is associated with a reduction of postnatal growth retardation. The authors assessed the growth of 84 preterm infants with a gestational age less than 30 weeks, who received parenteral energy intake above 50 kcal/kg/day. Of the enrolled infants, 67% showed mean values of weight and head circumference above the 10th percentile for intrauterine growth at 36 weeks of corrected age. In addition, increasing evidence indicates that lipids not only play an important nutritional role as a source of energy and precursors of long chain polyunsaturated fatty acids but may also positively affect later neurodevelopmental outcome [14].

With regard to protein intake, a linear relationship between protein intake and nitrogen retention in the early postnatal period has been reported [15]. In particular, considering that an intake of 1.5 g/kg/day on parenteral nutrition is required to prevent a negative nitrogen balance, it is recommended to start with a dose of 1.5-3 g/kg/day with increments up to 4 g/kg/day within the next few days [16]. Enteral protein requirements range from 3.5 up to 4.5 g/kg/day in the infants with the lowest birth weight [16,17].

When feeding the preterm infant, it must be taken into account that, in order to accomplish intrauterine growth rates, as recommended by the American Academy of Pediatrics [11], both adequate protein and energy intake must be supplied. In particular, it has been demonstrated that a protein intake of 3.5-4 g/kg/day is adequately supported by an energy intake equal to 115-120 kcal/kg whereas higher energy intakes lead to a disproportionate deposition of body fat mass [16].

An altered body composition, in addition to postnatal growth failure, has been found in preterm infants at hospital discharge or reaching term-corrected age; these findings highlight that the achievement of a growth pattern, not only in terms of quantity, but also in terms of quality, is a difficult task to achieve [18,19]. Roggero *et al.* [18] assessed body composition in 110 preterm infants at term-corrected age by air displacement plethysmography and reported a percentage of body fat content exceeding that of full-term infants (14.8±4.4 vs 8.59±3.71; P<0.0001). Cooke *et al.* [19] found that fat mass of the preterm infants, assessed by DEXA, was higher than that of the reference infant of similar mean body weight (13% ±3.4 vs 8.1%). Uthaya *et al.* [20] evaluated body adipose tissue using magnetic resonance imaging in 38 preterm infants at term-corrected age. The authors found that the preterm infants had a higher percentage of intra-abdominal internal adipose tissue volume as

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compared to the full term infants (4.62 vs 3.11; 95% CI−1.92 to−1.10; P<0.001, respectively). Contrary to these findings, Roggero *et al.* [21] reported that, in the absence of severe illness during the hospital stay, prematurity, although associated with increased total body fat mass, does not appear to be associated with a relative increase in intra-abdominal adipose tissue compared to term infants. A metanalysis published in 2012 pointed out that preterm infants at term-corrected show a substantial lack of fat free mass that could be partially due to an insufficient availability of nutrients during hospital stay [22]. The lack of fat free mass appears to track into childhood [23-25].

To which extent the recovery from postnatal growth retardation and the differences in body composition may affect health in later life is still under investigation. Indeed, considering the strict interrelationship existing between early nutrition and growth and subsequent health, concern has arisen that the advantage gained in the short term, when recommended intakes are adequately provided may imply a long-term cost with regard to the development of adult morbidities. As a result, the opportunity of promoting catch-up growth in preterm infants has been questioned.

With regard to these issues, however, it must be pointed out that, up to now, we have thought that the increased risk reported for infants born at term, with a low birth weight, to develop the metabolic syndrome in adulthood due to poor fetal growth and subsequent postnatal catch-up growth could be referred also to the preterm infants as they are usually born with a low birth weight [26].

It's now time to consider the preterm infant as a biological entity different from that of the low birth weight infant born at term as the preterm infant completes organogenesis being exposed to a non-physiologic environment and has peculiar nutritional needs. Hence, the effect of preterm birth itself, associated co-morbidities, nutrition and subsequent growth on the risk for developing obesity, hypertension and insulin resistance later in life needs to be further elucidated.

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