Improving the Neurodevelopmental Outcomes of Low-Birthweight Infants

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Low birthweight (LBW) infants comprise a heterogeneous group of infants born weighing <2,500 g. LBW can result from preterm birth, intrauterine growth restriction, or both. Whatever the reason, infants who are born with LBW are more likely to have lower scores on neurodevelopmental tasks into childhood compared with normal-birthweight term-born infants [1].

Preterm infants are at particular risk for long-term cognitive and educational problems directly proportional to their degree of prematurity, with those most preterm demonstrating a mean intelligence quotient (IQ) of 0.8–1.5 standard deviations (SD) lower than children who were born at term [2]. Children born full term and with LBW are twice as likely to have an IQ that is 2 SD lower than term-born appropriately grown infants [3]. Recent evidence also suggests there are higher rates of developmental delay in preterm infants born growth restricted compared with appropriately grown preterm infants [4, 5].

Strategies to improve the neurodevelopmental outcome of children born with LBW are important, and many interventions have focused on nutritional approaches applied during the postnatal period. This is an obvious strategy as high dietary requirements are implicated. Preterm infants are born before completion of the rapid nutrient accumulation during the last trimester of pregnancy, while infants who are growth restricted in utero have experienced some form of nutrient deprivation. Randomized controlled trials have investigated whether supplementation with long-chain polyunsaturated fatty acids (LC-PUFA) or dietary enrichment with protein and energy during the post-birth period improves the neurodevelopmental outcome of LBW infants.

Long-Chain Polyunsaturated Fatty Acids

Supplementation of infant formula with LC-PUFA for preterm infants has recently been systematically reviewed [6, 7]. Both reviews
found that supplemented formula had no significant effect on developmental quotients (DQ) compared with no supplementation. When trials using the same version of the Bayley Scales of Infant Development were considered as a separate subgroup, the cognitive DQ of LC-PUFA-supplemented infants assessed using version II of the Bayley Scales was significantly higher than control [7].

Two recent trials using doses of DHA reflective of the estimated in utero accretion rate and including infants fed human milk reported improvements in neurodevelopment [8, 9]. The best evidence comes from the largest trial [9]. Although there were no significant differences in overall cognitive DQ at 18 months’ corrected age, severe mental delay was halved, and girls had a significant 5-point (=0.3 SD) improvement in cognitive DQ [9].

**Protein and Energy**

Investigations of protein and energy enrichment date back to the 1960s. Few studies have measured neurodevelopment, so it is difficult to ascertain a confident and precise estimate of the effect of protein and energy enrichment. However, standard term formula and unsupplemented human milk are now regarded as nutritionally insufficient for preterm infants, and the focus has turned to protein concentration and post-discharge feeding.

The effect of higher protein early in the postnatal period on neurodevelopmental outcome has only been assessed in three trials [10]. In the studies where energy was controlled, there were mixed results with no difference in one trial and improved neurodevelopment in another [10]. In an early trial of very high protein supplementation (6–7 g/kg per day), lower IQ was found in early childhood when compared with standard protein (3–3.6 g/kg per day) [10]. The effects of feeding preterm infants with nutrient-enriched formula following hospital discharge has not resulted in reports of neurodevelopmental benefit [11].

In term infants born with LBW, standard versus nutrient-enriched formula showed poorer neurodevelopment in girls at 9 months of age with no difference in boys or girls at 18 months of age; additional evidence is needed before nutrient-enriched formula can be recommended for term LBW infants [12].

Further large-scale rigorously designed intervention trials with long-term neurodevelopment follow-up are required to determine the optimal nutritional supplements and the timing of their administration to LBW infants.
References