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Nutrition and Its Impact on Psychosocial Child Development: Preterm Infants

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Introduction

Advances in technologies for the support of preterm (<37 weeks gestation), low birthweight (<2,500 grams), and very low birthweight (<1,500 grams birthweight) infants following delivery and during care in intensive care units has led to a dramatic increase in survival rates. Poor maternal nutrition and prenatal care, along with pregnancy complications affecting nutrient delivery to the fetus contribute to intrauterine growth retardation. Consequently, preterm and low birthweight infants are at increased risk for major handicaps, as well as below-average cognitive abilities and above-average behavioural problems at school age, even among infants without obvious neurological deficits. Volumetric measurements of brain regions in children born preterm have shown disproportionately smaller volumes of the sensorimotor cortex amygdala, hippocampus, basal ganglia, and impaired development in other areas associated with lower cognitive abilities, behavioural problems, and an increased risk of ADHD (Attention Deficit Hyperactivity Disorder).[1,2] Hypoxic, metabolic, and nutritional insults are among the important factors that contribute to growth and developmental problems in these infants. Problems in

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providing and sustaining the optimal nutritional environment for the rapidly developing third trimester brain *ex utero* and during post-term infant development are likely to contribute to these developmental delays.

Problems

Our current understanding of the nutrient requirements of preterm and IUGR (Intrauterine Growth Retardation) infants is incomplete. On one hand, the transfer of nutrients across the human placenta is difficult to study, on the other hand, the requirements of preterm infants are markedly different from those of the fetus, owing to the need to facilitate the maturation and functioning of postnatal organ systems (eg, lungs, intestines), and to provide nutrition via the intestine (through the digestion, absorption, and metabolic assimilation of complex molecules). Nutrient delivery is often compromised by volume restrictions during early hospitalization, and concurrent drug treatments, in addition to immaturity, alter an infant's metabolism. Hypoglycaemia, including asymptomatic neonatal hypoglycaemia, increases the risk of reduced mental and motor developmental scores in preschool children.[3] The nutritional needs of preterm infants are not met by human breast milk, formulas designed for term infants, or parenteral nutrition. Most preterm infants with <29 weeks of gestation are discharged from hospital with significant growth retardation,[4] and due to a lack of well-developed resources to maximize catch-up growth potential, deficits in height, weight, and head circumference continue throughout childhood.[5-7] Deficits in growth and head size are associated with poorer educational and cognitive outcomes.[7] Children whose growth is restricted during their first two years of life score significantly lower than do non-growth restricted children on a wide range of cognitive tests, and although their scores can be improved through psychosocial stimulation, performance remains comparatively impaired.[8]

Key Research Focus

The requirements for classical nutrients and other biologically active dietary factors that maximize the developmental potential of the human brain, together with development of clinical products to provide these in parenteral and enteral nutrition are key research foci. Clinical products and practices should be developed to provide optimal nutritional support and prevent neural and physical growth stunting, while supporting and encouraging feeding with the mother's milk through at least the first 4 to 6 months post term. Research should be conducted to develop effective strategies for early identification and intervention of at-risk infants

experiencing feeding and growth difficulties, and potential micronutrient deficiencies.

Research Context

The transition from the neonatal intensive care unit to home can be stressful. Preterm and very low birthweight infants often have unpredictable behaviour and have a variety of problems which result in feeding difficulties.[9] Most preterm infants born after <29 weeks of gestation are discharged from hospital with significant growth retardation.[4] Post-discharge growth impairment is common and its onset can be remarkably rapid.[6] Due to a lack of well-developed identification and intervention resources, catch-up growth potential is not achieved in many preterm infants and deficits in height, weight, and head circumference continue throughout childhood.[5,6,7] Assessments of growth during the first three years assessed by adjusted (rather than chronological) age,[10] and attention to feeding and nutrition are essential elements in combating deficits in growth and failure to achieve catch-up.

Recent Research Results

The impact of nutrition on the psychosocial development of children born prematurely has been the subject of observational studies, case-control studies, and randomized trials with specific nutritional interventions. A meta-analysis of case-control studies of preterm infants evaluated after their 5th birthdays shows significantly lower weighted mean differences in cognitive scores of 10.9 points in preterm compared to control-term infants, and a greater prevalence of internalizing and externalizing behaviours and ADHD.[11] Mean cognitive test scores are lower among children of lower gestational age and lower weight at birth. Similarly, cohort studies have shown that preterm infants are at serious disadvantage for reduced school performance, requiring more special education and experiencing more behavioural problems than children born at term.[12]

Linguistic skills, including comprehension of logical grammatical constructions, phonemes and word fluency are also poorer in preterm infants[13] and recent work has suggested an increased risk of everyday memory difficulties at 5 years of age in children born before 32 weeks gestation.[14] Newer imaging techniques have shown reduced volumes in sensorimotor and other brain regions in preterm infants (even in the absence of reduced head size), which are related to cognitive deficits.[1,2] Neonatal nutritional support includes the dramatic shift from transplacental to intravenous or alimental nutrient delivery; periods of energy, macronutrient, and

micronutrient deficits; metabolic complications such as hypoglycaemia; and the use of drugs such as steroids, which profoundly alter nutrient metabolism and head growth. Deficits in energy and essential nutrients during brain growth can impair cell division, myelination, and neural functional development.

Human milk and formulas for term infants do not meet the high nutrient and energy needs of preterm or low birthweight infants. Feeding nutrient-enriched formulas with higher protein, energy, calcium, phosphorous, iron, zinc, and other micronutrients reduces deficits in motor and mental developmental indices at 18 months, with the advantage in verbal and overall IQ maintained at school age.[15] Feeding nutrient-enriched formulas post-discharge for 9 months or longer also improves nutritional status, linear growth and occipitofrontal head circumference gains in preterm infants.[16] Preterm infants are at risk of deficiency with regard to many nutrients which are critical to central nervous system development. Irrespective of weight for gestational age, preterm infants show evidence of iron deficiency before 4 months post-term, whereas term infants do not show iron deficiency at this age.[17] Iron deficiency (even in the presence of iron therapy) during infancy impairs a variety of cognitive processes and increases behavioural problems, persisting into later childhood.[18] A meta-analysis of data from randomized studies with preterm infants fed formulas supplemented with the long chain essential fatty acids, docosahexaenoic acid and arachidonic acid (which are crucial components of retinal and neuronal membranes) has shown a significant benefit in visual development.[19] Randomized controlled trials have also shown a significant advantage in psychomotor and language developmental tests among preterm newborns weighing <1250 grams supplemented with these fatty acids.[20]

Conclusions

Our current understanding of the biological, environmental, and psychosocial mechanisms involved in the cognitive and behavioural deficits of preterm children is incomplete. Failure to provide and sustain the energy, protein, and essential micronutrients needed to support the complex process of human brain development is an important contributing factor. Therefore, improved strategies are required for early identification and intervention in growth and feeding problems, and the development of feeding strategies to provide the nutrient enrichment needed to maximize potential for catch-up.

Implications

The decrease in cognitive test scores of 9 to 10 points in meta-analysis,[11] broad-based behavioural problems, and increased prevalence of ADHD among preterm infants have profound implications for concerned individuals and populations. Available data indicate that preterm children are 50% more likely to be enrolled in special education classes, and when extrapolated from US data from 1988,[21] this intervention alone conservatively costs an extra $37 million per year in Canada.

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