Nutrition and Its Impact on Psychosocial Child Development: Perspective on Preterm Infants

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Topic
Breastfeeding
Nutrition and pregnancy
Prematurity

Introduction
The profound impact of nutrition on the early growth and body composition of low birthweight (LBW) infants is well known.[1] Emerging evidence supports the thesis that both the quantity and quality of nutrients delivered in early life to LBW infants affects infant and child development and underlines the need for a renewed emphasis on optimizing early nutrition. Intrauterine and postnatal growth restrictions are associated with a myriad of adverse outcomes in LBW infants, even at adolescence, including short stature, disproportionately small heads and sub-optimal weight in relation to age.[2,3] In turn, deficits in growth have been associated with poor educational and cognitive outcomes,[4,5] including low verbal and performance IQ scores and inappropriate receptive language, speech, reading, math, and spelling skills in children,[6,7] or risk of schizophrenia.[8]

Subject
The relationship between early nutrition and neurodevelopment has come to the fore once again through investigations into the influence of feeding (human milk compared to bovine-based formula) and specific nutrients, such as the long chain polyenoic fatty acids (LCPUFA), on developmental outcomes in LBW infants.

Problems
Mounting evidence supports the view that LBW infants who are fed their mother's milk early in life have greater visual acuity, language skills and developmental outcomes (up to at least 18 months of age) than do comparable groups of infants fed bovine-based infant formula. Research continues on the specific nutrient(s) or socio-environmental factors related to feeding practices that effect the observed developmental advantages.

Research Context
The influence of feeding with mother's milk compared to formula on developmental outcomes has been studied both retrospectively and prospectively, although from an ethical standpoint it cannot be designed through randomized trials. Reported studies vary

in the degree to which they have adjusted their analyses for confounding factors (such as socio-economic status), differences in demographic characteristics (such as parental education and smoking), size at birth, parenting skills, and the proportion of breast milk intake in relation to total feeding volume. To date, investigation of the nutrient(s) possibly responsible for the observed benefits of mother's milk on neurodevelopment have focused on the LCPUFAs, docosahexaenoeic acid (DHA), and arachidonic acid (AA), since they represent the greatest proportion of LCPUFA contained in the phospholipids of neural and retinal tissues and are naturally present in human milk. Until very recently LCPUFAs were not present in infant formulas as they are not natural components of the vegetable oils used in the manufacture of formula. The lack of a dietary source of LCPUFAs may be of concern for LBW infants who, due to their immaturity, may have a limited capacity to synthesize them from the essential linolenic and linoleic fatty acids. Most reported studies that have investigated the efficacy of adding LCPUFAs to infant formulas are randomized double-blind clinical trials often including a reference group of breast-fed infants. However, a comparison of findings is complicated by inconsistencies in studies regarding the duration of nutrition intervention, variability in the source of DHA/AA (single-cell triglycerides, marine oil, evening primrose oil and/or egg lipids), the amount of DHA/AA added, and the inclusion of a reference control group of either term or premature infants who were fed their mother's milk.

Key Research Questions

The key research question is whether feeding LBW infants their mother's milk in early life benefits neurobehavioural development, which in turn, affects intellectual programming and social behaviour; and if so, by what mechanism (nutrients and/or feeding behaviours) this outcome occurs. If nutrients unique to human milk – such as one or more of the LCPUFAs - are thought to be the mediators of benefits to neurobehavioural development, then the sequential research question is whether addition of those nutrients to infant formulas will elicit the same developmental benefits.

Recent Research Results

The positive benefits of breastfeeding compared to formula feeding on short-term visual and developmental outcomes in both term and LBW infants have been observed in several studies (as summarized in reviews by Anderson et al. and Jain et al.[9,10]). Based on a meta-analysis of six studies, LBW infants derived greater benefits from breast feeding than did normal-weight infants,[9] with the breastfed (N=1294) compared to formula-fed (N=751) infants recording a significant ($p<.001$) 5.18 point advantage (compared to a 2.66 point advantage for term born infants) in a cognitive development score. As noted above, inconsistency exists across studies in measures of confounding variables and may impact test scores (eg, maternal IQ, birth order, and paternal education). Comparability between reported studies is further hindered by variability in the definition of breastfeeding (ie, exclusivity and duration), the use of nutrient supplements or fortifiers for human milk, and the ages at which outcomes are measured. Since a dose-response relationship has been established between human milk intake and developmental outcomes,[9] the daily intake and duration of breastfeeding are important variables that should be measured in such studies. Major changes in nutritional practices for LBW

infants over the past 20 years may have had a significant influence on developmental outcomes. For instance, in a British study reported in 1992,[11] infants who were fed donor, unfortified breast milk versus term formula, demonstrated an advantage of up to 8.8 points difference in psychomotor scores (Bayley Scales of Infant Development) and of 2.1 points in mental development scores. In contrast, when the same group studied LBW infants fed diets more reflective of neonatal practices today (ie, human milk with a multinutrient fortifier containing protein, human milk supplemented with minerals alone or premature formula), they found that the neurodevelopmental outcomes for this group at 18 months were not statistically better in the infants fed fortified human milk.[12]

The biological basis for feeding infants human milk early in life to produce positive neurodevelopmental outcomes is uncertain, but DHA and AA, which have their greatest effect on the rapidly developing immature brain, appear to be the key elements for consideration. More than a dozen clinical trials have compared feeding LBW infants formulas that contain DHA±AA to feeding them formulas that do not contain these nutrients, with some trials including a breastfed reference control group. A Cochrane systematic review[13] concluded that no long-term benefit was derived from supplementing formula with DHA, with the possible exception of benefit to accelerating the rate of early visual maturation. Since this review, three reported randomized clinical trials with reasonably large sample sizes produced inconsistent results. Positive benefits to visual acuity,[14,15] language, and developmental outcomes[14] were observed in preterm infants fed formula with added DHA and AA for at least 28 days in early life. In a study of similar design[16] the addition of DHA/AA produced no significant effect in cognitive and motor development up to 18 months of age in former preterm infants. In both studies, breastfed reference infants demonstrated outcomes of visual acuity or neurodevelopment that were significantly more advanced than infants receiving the formula supplemented with DHA/AA. Deficits in growth, in weight and/or length among infants fed formula supplemented with LCPUFA have been observed inconsistently, but Simmer[13] concluded there was no overall negative impact on growth among infants fed such formulas. Nevertheless, a recent randomized trial in the United Kingdom revealed that even 18 months after the completion of the dietary intervention of formula supplemented with DHA+AA, a significant growth deficit in the length of infants was observed.[16]

Conclusions

While the precise role of early life nutrition in the neurodevelopmental outcomes of LBW infants is not well defined, emerging evidence suggests that feeding infants their mother's milk benefits developmental outcomes that can be measured up to 9 years of age. While the size effect is small, the potential for enhancing child development at no risk and little cost may be especially important for premature infants, who are prone to developmental difficulties. Future research should explore whether the neurodevelopmental advantages observed in breastfed infants are linked to psychosocial or environmental factors, or to select nutritive and non-nutritive factors in human milk, rather than to absolute intakes of protein or energy. The addition of LCPUFA to formulas for LBW infants also needs to be more fully explored both for efficacy and safety.

Implications for Policy and Services

Awareness of the impact of early nutrition on the neurobehavioural development of LBW

infants is essential if we are to implement the objectives of the 1999 *Second Report on the Health of Canadians — Toward a Healthy Futures*, which states: "The foundation for healthy growth and development in later years is established to a large degree in the first six years. […] Efforts are needed to maximize all children's opportunities for healthy development." Research to date supports current recommendations that LBW infants be fed their mother's milk. Future development of powdered fortifiers for mother's expressed milk and formulas specifically designed for LBW infants should take the influence of specific nutrients on neurodevelopment and not just somatic growth into consideration. In order to adequately assess the efficacy of such products, we may have to develop tests that are more sensitive measures of diet-induced alterations in behavioural and cognitive functions, both in early life and at school age.

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