Role of Long-Chain Polyunsaturated Fatty Acids in Growth and Development

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The synaptosomal membranes of the central nervous system contain high concentrations of the n-3 long-chain polyunsaturated fatty acid (LCPUFA), DHA (22:6 n-3). Animal studies show that diets deficient in n-3 fatty acids are associated with reductions in brain DHA concentrations, decreased dopamine and serotonin, reduced neuronal cell size as well as decreased visual function, impaired visual recognition memory, and compromised learning behavior [1]. In 1990 the first publication in human infants was consistent with the findings from animal studies and showed that preterm infants fed a formula supplemented with n-3 LCPUFA, mainly as DHA, had improved retinal sensitivity compared with preterm infants fed the standard unsupplemented formula of the day [2]. Since then, there has been an explosion of interest in the role of LCPUFA in growth and development of all infants. In 2009 there are at least 12 published randomized controlled trials (RCTs) assessing the effects of LCPUFA supplementation of infant formula for preterm infants and 17 RCTs involving formula-fed term infants. In addition, at least 5 RCTs have investigated the effect of increasing the DHA concentration of human milk through maternal supplementation on indices of infant and early child development and several are actively investigating the effects of DHA supplementation during pregnancy. This degree of research activity has resulted in a wealth of quality information regarding the effects of LCPUFA on infant growth and development. Collectively the published literature has been free of reports of harm from dietary LCPUFA for infants, although the consistency of benefit has been less clear. Some trials report positive effects of LCPUFA supplementation at multiple time points, others report positive effects at some ages but not others, while some report no effects at all.
Which LCPUFA?

Many studied supplements containing a combination of DHA and arachidonic acid (AA, 20:4n-6), an n-6 LCPUFA. This has been a result of early fears of compromised growth when preterm infants were fed formulas containing only n-3 LCPUFA that resulted in a depression of plasma AA [3]. It was hypothesized that n-3 LCPUFA supplementation may have been causative to the growth deficit. However, this hypothesis has not been substantiated [4]. Furthermore, there are no consistent data to suggest that there are differential effects of infant development if DHA is used alone or in combination with AA.

When to Supplement?

DHA accretion is predominantly to neural tissues and peaks during the fetal brain growth spurt in the last trimester of pregnancy. This may explain why LCPUFA supplementation trials consistently demonstrate developmental benefits in preterm infants, while the observations from studies involving term infants are less clear.

As many pregnant women in Westernized countries have low dietary intakes of DHA there is now increasing international interest in whether higher DHA intakes during pregnancy also benefit the cognitive outcomes of infants born at term. Although cohort studies show that maternal intake of foods rich in DHA during pregnancy are positively associated with cognitive development, motor function, language and behavior in early life, conclusive evidence from RCTs is lacking.

Which Dose?

The new phase of LCPUFA research is focusing on dose. We recently demonstrated that DHA given at a dose designed to approximate the in utero accumulation rate (3 times the standard dietary dose) resulted in fewer preterm children with significant mental delay at 18 months corrected age compared with control (5.2 vs. 10.5%; p = 0.03) [5]. The effect was most pronounced in girls born <33 weeks gestation and in infants born weighing <1,250 g [5] but there was potential for further improvements. These data have raised new questions about DHA dose as well as its timing. Although we have answered many questions in LCPUFA nutrition, many still remain.
References