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Review Article

DHA, LCPUFAs, ARA Nutrition Musketeers for Early Infancy and the Role in The Eye & Brain Growth and Development

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Abstract

DHA – and other long-chain polyunsaturated fatty acids (LCPUFAs) like arachidonic acid (ARA) – have received well-deserved recognition in the world of nutrition for the role they play in early development [1], and, for their role in brain and eye development. In this mini review, let's dig into the science behind DHA and find out why this omega-3 fatty acid is such a critical part of nutrition early in life.

DHA is an omega-3 fatty acid involved in several aspects of our physiology and metabolism. It is a key component of certain tissues and membranes in the body – which means adequate amounts of it can play a crucial role in development. Specifically, during infancy, DHA plays a central role in the development of the brain, eyes, and immune system.

The long-chain polyunsaturated fatty acids (LCPUFAs) Arachidonic Acid (AA) and Docosahexaenoic Acid (DHA) are important components of breast milk.

Immune markers in preterm and term infants fed formula with AA and DHA were like those in infants fed human milk, whereas those in infants fed formula without LCPUFAs were not. Infants who received formula plus LCPUFAs (both AA and DHA) showed a reduced risk of allergic disease and respiratory illness than infants who received standard formula.

Studies in which infants received n-3 LCPUFAs report immune differences from controls that suggest better immune maturation and they show lower risk of allergic disease and respiratory illness over the first years of life. Taken together, these findings suggest that LCPUFAs play a role in immune development that is of clinical significance, particularly regarding allergic sensitisation and allergic manifestations including wheeze and asthma.

Keywords: DHA; AA; LCPUFAs; Brain growth; Infant formula; IQ; Immune development

Introduction

Docosahexaenoic Acid (DHA) and Arachidonic Acid (AA) are important to foetal and infant growth and development. Observational and intervention studies provide consistent evidence that maternal dietary and circulating DHA is an important determinant of foetal blood concentrations of DHA [1-6]. Although Linoleic Acid (LA) and α-Linolenic Acid (ALA), and preformed long chain polyunsaturated fatty acids (LCPUFAs), can be transported through the placenta, there is a preferential transfer of the latter forms [6-7]. Several studies have assessed the effect of prenatal LCPUFA dietary supplementation on pregnancy outcome, aiming to improve it. i.e., preventing preeclampsia, prolonging gestation, preventing preterm birth, and improving foetal growth [3,8,9].

On the other hand, the importance of DHA in Central Nervous System (CNS) development is one of the most intensely studied areas [10-14]. DHA functions in neurogenesis, neurotransmission, and protection against oxidative stress [15]. AA is also important for infant growth and development. n-3 and n-6 LCPUFA are critical for infant and child brain development; they are involved in numerous neuronal processes, ranging from effects on membrane fluidity to gene expression regulation [16]. Brain accumulation of DHA starts in utero, with quantitatively marked deposition in the second half of gestation [17-19], coinciding with the growth spurt in the grey matter [19]. Deficiencies and imbalances of LCPUFAs are associated with impairments in cognitive and behavioural performance [20].

Fish intake during pregnancy and a higher n-3 LCPUFA status at birth were associated with a better visual development in infants born at term [20-22]. However, levels of DHA and eicosapentaenoic acid (EPA) are often low in the Western diet [23-24]. It remains controversial whether LCPUFA supplementation to pregnant and breastfeeding mothers is beneficial for the development of their infants [25-26], optimal doses for efficacy and long-term effects at different developmental ages remain to be determined. Today, there are more than 40 perinatal randomized controlled trials involving LCPUFA interventions assessing different aspects of early childhood development and growth [29].

The earliest publications in human infants from the early 1990s showed that preterm infants fed a formula supplemented with n-3 LCPUFA, mainly as DHA, had improved retinal sensitivity and visual acuity compared with preterm infants fed the standard un-supplemented formulas of the day, which were low in n-3 PUFA (most were lacking alpha-linolenic acid) and were rich in n-6 PUFA [28-30]. Other intervention studies have also provided evidence that dietary DHA improves visual, mental, and motor skill development in some preterm and term infants fed supplemented formula [31].
In a non-randomised observational study, term infants fed breast milk have been found to have more mature visual acuities and correlated to higher erythrocyte DHA levels than those receiving formula [31]. Evidence to suggest that breastfed infants have a long-term IQ advantage over those who have been fed formula has been evident in the literature for many years. Moreover, we realize that the majority of comparisons between breast fed, and formula-fed infants are confounded by genetic polymorphisms that affect LCP metabolism and socioeconomic factors which affect the outcomes of most studies [31].

DHA and brain health
The brain accumulates large amounts of DHA before birth [32] – primarily in the third trimester – as well as after birth. DHA uptake by the brain is highest during the first two years of life, a period when the brain is rapidly growing. In fact, the brain growth that occurs before your little one's second birthday will be faster than any other time in their life! This early stage represents a critical window of time when optimal nutrition is so important for supporting development [33].

DHA and eye health
DHA is also the predominant fatty acid in the retina of the eye. The retina (34) is responsible for visual recognition by receiving and organizing visual information; it then sends signals from the eye to the brain, allowing us to see. In addition to supporting healthy development of the retina, DHA may also offer a protective role to this fundamental tissue in our eyes.

DHA and the immune system
There is some evidence that DHA and ARA might play a role in supporting the immune system, especially during early infancy when the immune system is rapidly developing.(35) In fact, researchers found that infants fed a formula supplemented with DHA and ARA in the new born period had markers of immune function(36) that were similar to those of breastfed infants.
What are the health benefits of DHA?
DHA has been extensively researched over the last few decades, and, to help scientists understand how this fatty acid impacts infant growth and development. The findings from preclinical and clinical trials on DHA – alongside another LCPUFA, ARA – led to the addition of DHA and ARA in infant formulas, a critical innovation in infant feeding.

Some of the most important discoveries around why DHA is so important are highlighted here:

1- DHA and ARA supplementation in infants has been shown to positively impact cognitive development, even beyond the period when the formula was consumed. In one study, infants who received infant formula supplemented with DHA and ARA through four months of age were faster at processing information at six years of age compared to the group who didn't receive DHA and ARA in infancy [37].

2- Also suggesting that DHA and ARA impact brain development, in a study assessing mental adaptability and flexibility in three-year-olds, children who received the recommended dose of DHA and ARA supplementation had improved scores compared to those who received less than optimal doses [38].

3- Clinical studies have demonstrated that DHA and ARA supplementation in infants improved visual acuity [39] during the first year of life, compared to those who did not receive supplementation. Of note, the findings were based on a specific amount of DHA, 0.32% of total fat, an amount that reflects amounts of DHA found in breast milk. This illustrates that the amount of DHA in baby formula matters!

4- Long-term follow-up of infants who received supplemental DHA and ARA in infancy found that, at four years of age, their visual acuity was similar to what was observed in breastfed infants, which represents the gold standard in infant feeding [40].

The benefits of DHA are seen beyond infancy – research has uncovered positive benefits of DHA and other omega-3 fatty acids in older children and adults as well. Heart health benefits have been observed when DHA is supplemented alongside another omega-3, Eicosapentaenoic Acid (EPA). DHA may also help reduce inflammation, support eye health in adults, and regulate behaviour and attention in people with Attention Deficit Hyperactivity Disorder (ADHD).

Conclusions
As nutrition research continues LCPUFAs, scientists are learning that the presence of both DHA and ARA in infant formula are critical. In addition, the ratio of DHA:ARA also matters. Studies have found positive outcomes when ARA is at least at equal concentration to – and up to twice the amount of – DHA. Higher or lower ratios of ARA to DHA may not yield benefits. Experts agree on the importance of providing both DHA and ARA in infant formula [41].

Recommended intakes of DHA in the US and Europe

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Recommended intake of DHA in infancy	
US National Institutes of Health (NIH)	Guidance not provided*
European Food Safety Authority (EFSA)	100 mg/day (0 to 6 months of age)
Regulations for DHA in infant and follow-on formula	
US Food and Drug Administration (FDA)	Optional ingredient; not required
EFSA	20-50 mg per 100 kcal

There are definite differences between the US and Europe when it comes to recommended intakes of DHA in infancy, as well as the regulations around the addition of DHA to US infant formula [42].
the US NIH recommends 0- to 12-month-olds consume 500 mg per day of omega-3 fatty acids but does not provide guidance for DHA intake specifically.
Alpha-linoleic acid (ALA) is the "parent" fatty acid to DHA. Our bodies, through a series of complex steps, can convert ALA into DHA. However, in general, we don't do this very efficiently. Further, some people – depending on genetics – have very low rates of converting ALA to DHA at all. For this reason, it's important that DHA is consumed directly in the diet. Therefore, infants rely on breast milk or infant formula for their DHA [43].

There is some evidence that DHA and ARA might play a role in supporting the immune system, especially during early infancy when the immune system is rapidly developing. In fact, researchers found that infants fed a formula supplemented with DHA and ARA in the new born period had markers of immune function that were similar to those of breastfed infants.

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