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DHA and human infants

The importance of polyunsaturated fatty acids, especially DHA, in human eye and brain function has been most thoroughly researched with respect to infant nutrition (Gibson, Chen and Makrides 2001, San Giovanni, Parra-Cabrera, Colditz et al 2000) and numerous reviews of trials on full term and preterm infants have been published. Reviews of preterm studies are virtually unanimous in concluding that the available evidence supports a role for preformed dietary DHA in the visual and neural function of preterm infants (Hoffman, Birch, Birch et al 1993, Crawford 1993, Uauy-Dagach, Mena and Hoffman 1994, Crawford, Costeloe, Ghebremeskel et al 1997, 1998, Uauy and Mena 1999, Uauy and Hoffman 2000)

A recent paper by Lapillonne and Carlson (2001) mentions early work on preterm infants, which seemed to indicate that those fed EPA and DHA had reduced growth achievement compared to controls (Carlson, Cooke, Werkman et al 1992). To examine this issue, the review considers 32 randomised trials, 13 in preterm infants and 19 in term infants. It was concluded that 'from the data published to date, it seems clear that long-chain n-3 fatty acids can reduce growth achievement in preterm and term infants under some experimental conditions. However, the effect of n-3 PUFA supplementation on the growth of preterm and term infants appears to be minimal and of questionable clinical and/or physiologic relevance'. Tolley and Carlson (2000) discuss experimental design in studies of DHA and visual acuity development.

The following papers report trials related to LCPUFA nutrition of preterm infants:

Carlson, Rhodes and Ferguson (1986)
Uauy, Birch, Birch et al (1990)
Birch, Birch, Hoffman et al (1992)
Lucas, Morley, Cole et al (1992)
Birch, Birch, Hoffman et al (1993)
Hoffman, Birch, Birch et al (1993)
Carlson, Werkman, Rhodes et al (1993)
Carlson, Werkman, Peeples et al (1994a)
Carlson, Werkman, Peeples et al (1994b)
Uauy, Hoffman, Birch et al (1994)
Carlson, Werkman and Tolley (1996)
Faldella, Govani, Alessandroni et al (1996)
Uauy, Peirano, Hoffman et al (1996)
Werkman and Carlson (1996)
Clandinin, Van Aerde, Parrott et al (1997)

Bougle, Denise, Vimard et al (1999)
Clandinin, Van Aerde, Parrott et al (1999)
Hoffman, Birch, Birch et al (1999)
Koletzko, Knoppke, Von Schenck et al (1999)
Vanderhoof, Gross, Hegyi et al (1999)
Woltil, Van Beusekom, Schaafsma et al (1999)
O'Connor, Hall, Adamkin et al (2001)

While most studies indicated a clear benefit, the study by Bougle, Denise, Vimard et al (1999) was unusual in that it found no significant difference in measures of visual, auditory and nerve function between three groups of preterm infants fed breast milk or formula containing only 18 carbon polyunsaturated fatty acids (PUFA) or long chain PUFA (including DHA and AA).

The importance of DHA in nutrition of full term infants has not been so clearly established, despite more numerous investigations. Some of the earliest studies of infant nutrition compared attainment score in breast fed infants with those fed with formula devoid of LCPUFAs and found that breast feeding resulted in higher scores (Rodgers 1978, Taylor and Wadsworth 1984, Morrow-Tlucak, Haude and Ernhart 1988, Temboury, Otero, Polanco et al 1994) and it was speculated that the difference could be due to lower DHA levels in formula-fed infants. Infants fed formula lacking LCPUFAs had significantly lower levels of DHA and AA in red blood cells and plasma compared to breast-fed infants (Ponder, Innis, Benson et al 1992, Thiel and Koletzko 1995). Post-mortem studies demonstrated deficiencies in infant brain, retina and blood DHA of formula-fed compared with breast-fed infants (Farquharson, Cockburn, Patrick et al 1993, Makrides, Neumann, Byard et al 1994).

Subsequent feeding trials demonstrated that blood LCPUFA levels could be increased to the levels found in breast-fed infants by supplementing infant formula with LCPUFA (Kohn, Sawatzki, Van Biervliet et al 1994, Makrides, Neumann, Simmer et al 1995, Innis, Auestad and Siegman 1996, Lapillonne, Brossard, Claris et al 2000, Maurage, Guesnet, Pinault et al 1998, Connor Zhu, Anderson et al 2000). Feeding trials have also investigated the effect on infant development, particularly in relation to visual acuity, of DHA and AA supplementation. More trials have demonstrated beneficial effects than those that did not show a benefit.

Papers on full term Infants showing a positive effect of LCPUFAs

Makrides, Simmer, Goggin et al (1993)
Innis, Nelson, Rioux et al (1994)
Lanting, Fidler, Huisman et al (1994)
Agostoni, Trojan, Bellu et al (1995)
Makrides, Neumann, Simmer et al (1995)
Carlson, Ford, Werkman et al (1996)
Agostoni Trojan, Bellu et al (1997)

Birch, Hoffman, Uauy et al (1998)
Courage, McCloy, Herzberg et al (1998a)
Willatts, Forsyth, Di Modugno et al (1998b)
Birch, Garfield, Hoffman et al (2000)

Papers on full term infants showing no significant effect of LCPUFAs

Auestad, Montalto, Hall et al (1997)
Innis, Akrabawi, Diersen-Schade et al (1997)
Jorgensen, Holmer, Lund et al (1998)
Scott, Janowsky, Carroll et al (1998)
Lucas, Stafford, Morley et al (1999)
Makrides, Neumann, Simmer et al (2000)
Auestad, Halter, Hall et al (2001)

Despite these negative papers the most recent reviews have concluded that the balance of evidence indicates LCPUFA nutrition is important in neural and visual development. Sangiovanni, Berkey, Dwyer et al (2000) concluded that 'dietary n-3 intake is associated with performance on visual resolution acuity tasks at 2 and possibly 4 months of age in healthy full term infants'. Uauy, Hoffman, Peirano et al (2001) concluded that the 'studies summarised in this review provide evidence supporting the view that essential fatty acid supply affects visual development of preterm and term infants'. A review by Uauy, Mena and Rojas (2000) concluded that 'Recent clinical trials convincingly support LCPUFA supplementation of preterm infant formulations and possibly term formula to mimic human milk compositions'. Gibson and Makrides (2000) conclude that 'because the LCPUFAs of breast milk appear to be dependent on maternal dietary LCPUFAs it …seems prudent to ensure that breast milk from mothers who include some fish in their diets is used to guide dietary recommendations for infants'.

Other reviews related to LCPUFA nutrition of full term infants are listed below:

Reviews on full term infants

Clandinin, Chappell and Van Aerde (1989)
Koletzko (1992)
Uauy, Birch, Birch et al (1992)
Uauy-Dagach and Mena (1995)
Bendich and Brock (1996)
Makrides, Neumann and Gibson (1996)
Gordon (1997)
Heird, Prager and Anderson (1997)
Gibson and Makrides (1998)
Carlson and Neuringer (1999)

Heird (1999)
Innis, Sprecher, Hachey et al (1999)
Kurlak and Stephenson (1999)
Cunnane, Francescutti, Brenna et al (2000)
Neuringer (2000)

In addition to direct studies on LCPUFA supplementation a number of trials have indicated that the ratio of linoleic acid to alpha-linolenic acid in formula feeds can influence the AA and DHA status of infants (Gibson, Makrides, Neumann et al 1994, Jenson, Chen, Fraley et al 1996, Makrides, Neumann, Jeffrey et al 2000). Another potential confounding factor in infant feeding trials is the LCPUFA status of infants at birth i.e. before supplementation begins (Guesnet, Pugo-Gunsam, Maurage et al 1999) while Makrides, Neumann and Gibson (2001) reported that a variety of perinatal characteristics including birth weight, gender and number of smokers in the household could influence the effects of diet on visual acuity measurements.

Conclusion

The balance of evidence suggests that dietary DHA is essential for healthy eye and brain development and function in the premature infant and probably also in the full term infant.