



Long-Chain Polyunsaturated Fatty Acids: The Case for and Against the Supplementation of Infant Formula

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DESCRIPTION

Infant formula's deficiency in preformed Long-Chain Polyunsaturated Fatty Acids (LCPUFA) has been theorized to be a factor in the cognitive disparities between breastfed and formula-fed newborns. Previous systematic reviews focused on early developmental measures, like the Bayley Scales of Infant Development, which are poorly differentiating and not predictive of cognitive ability in childhood, and found no cognitive differences between infants fed formula with LCPUFA and those fed formula without. In this systematic study, the impact of randomizing infants to formula with LCUFA supplements versus formula without supplements on cognitive performance at 2.5 years of age was investigated. Following a pre-published protocol in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) principles, they searched without date restriction Medline, Embase, and the Cochrane Central Register of Controlled Trials. To assess the quality of the evidence and the possibility of bias, they performed random effects meta-analyses in RevMan v5.4 while adhering to the GRADE and Cochrane Guidelines. Between 1993 and 2004, 8 trial cohorts randomly assigned participants. They examined 6 previously unpublished results supplied by various trialists. The age range at the most recent cognitive test was 3.3 to 16 years.

Wechsler Preschool and Primary Scale of Intelligence-Revised pooled mean differences from four studies in term-born children revealed no advantage of LCPUFA: 95% prediction interval: -14.17 to 14.25, 95% confidence interval: -0.04 points. Additionally, there was no advantage of LCPUFA in the pooled mean difference in Wechsler Abbreviated Scale of Intelligence score from two trials in preterm-born children: 9.22 (95% CI -24.63 to 9.22, 95% PI -97.80 to 82.38), or -7.71. Due to significant heterogeneity, short follow-up rates, and indications of selective publication, the overall quality of the evidence was low. The long-term impact of LCPUFA supplementation on cognition in term and preterm-born newborns is highly speculative and has the potential to have both significant positive and negative effects. Based on our findings, it is not advised to augment infant

formula with LCPUFAs until more reliable data rule out long-term harm. Docosahexaenoic Acid (DHA) and Arachidonic Acid (AA), two Long-Chain Polyunsaturated Fatty Acids (LCPUFA) that mostly accumulate during the third trimester of pregnancy and early infancy, are crucial structural elements of the human brain. While infant formula historically only contained the precursors alpha linoleic acid and linoleic acid, which infants, especially those born preterm, may not be able to properly synthesise into DHA and AA, human breast milk contains DHA, AA, and their fatty acid precursors.

According to research, children who are breastfed have better cognitive abilities than those who are fed formula. It has been hypothesized that the absence of preformed LCPUFA in newborn formula is a factor in these cognitive abnormalities. However, there is currently no conclusive proof from published Randomized Controlled Trials (RCTs) that infant formula with LCPUFA supplements enhances cognition in comparison to formula milk without supplements. Because they largely focused on early measures of cognition, like the Bayley Scales of Infant Development, earlier systematic evaluations of RCTs may have been unable to identify a difference in cognition. Early assessments of cognition, however, are insufficient to distinguish between cognitive abilities that might be impacted by nutritional supplementation and are not very accurate predictors of cognition over the school years. Later follow-up utilizing more trustworthy cognitive function indicators, such as IQ scores, may increase the likelihood of spotting an effect of LCPUFA supplementation. Given that the EU Commission (EC) has mandated the addition of one type of LCPUFA, DHA, to all newborn and follow-on formulae, clear data about the long-term consequences of LCPUFA-supplementation is required. Although the decision acknowledged the lack of evidence regarding cognitive benefits and was instead based on theoretical arguments, mandatory supplementation may lead to price increases across the market. A family can spend up to \$400 more annually on LCPUFA-supplemented infant formulas when compared to unsupplemented infant formula. To our

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knowledge, no systematic review has yet examined the effects of infant formula supplemented with LCPUFA on cognitive development in later childhood, when more precise measurements are available. The current investigation compares

the long-term cognitive effects of LCPUFA-supplemented with unsupplemented infant formula in infants born at term and preterm using published and previously unpublished trial data that was obtained by contacting trial authors.