Journal of Nutrition & Intermediary Metabolism 5 (2016) 34–54

Contents lists available at ScienceDirect

Journal of Nutrition & Intermediary Metabolism

journal homepage: http://www.jnimonline.com/

Omega-3 polyunsaturated fatty acid supplementation during the pre and post-natal period: A meta-analysis and systematic review of randomized and semi-randomized controlled trials

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ARTICLE INFO

Article history:
Received 1 December 2015
Received in revised form
20 April 2016
Accepted 26 April 2016
Available online 4 May 2016

Keywords:
Long-chain n-3 PUFA
DHA
Infant development
Formula
Breastfeeding
Maternal supplements

ABSTRACT

Background & Aims: Long chain omega-3 polyunsaturated fatty acids (n-3 PUFA), such as docosahexaenoic acid (DHA) are widely considered beneficial for infant health and development. The aim of this meta-analysis was to summarize the evidence related to the clinical outcomes of long chain n-3 PUFA supplementation maternally and in fortified formula/taken directly. Additionally, we investigate if the addition of arachidonic acid (AA) alters the effects caused by n-3 PUFA supplements.

Methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE (1974 to June 2015) CINAHL (1990 to June 2015), PubMed (1966–2015), Web of Science (1864–2015), MEDLINE (1974 to June 2015), and hand searches for randomized and semi-randomized controlled trials on term infants evaluating the effects of long chain n-3 PUFA supplementation taken maternally and in milk based formula or directly.

Results: We identified 39 formula and 39 breastmilk studies on the clinical outcomes of long chain n-3 PUFA supplementation, with or without AA, on infant immunity and development. Of these studies, 32 formula and 37 breastmilk studies were deemed appropriate resulting in a total of 2443 formula fed infants and 4553 breastfed infants exposed to n-3 PUFA supplementation. This meta-analysis shows that n-3 PUFA supplementation in infants delivered either maternally or in formula/directly, does not improve visual acuity, language development, or cognition. However, some aspects of growth, motor development, behavior and cardiovascular health are differentially altered in the summary effects of certain studies with the more desired effect occurring often in breastfed infants compared to formula fed infants. Moreover, this meta-analysis shows that n-3 PUFA supplements affects infant immune development and reduces pro-inflammatory responses in the supplemented breastfed and fortified formula fed/directly supplemented infants.

Conclusion: Overall, the evidence does not support the continued supplementation of infant formula with long chain n-3 PUFA considering the negative impact on the developing immune responses.

Contents

Abbreviations: n-3 PUFA, n-3 polyunsaturated fatty acid; DHA, docosahexaenoic acid; AA, arachidonic acid; ALA, alpha-linolenic acid; LA, linoleic acid.

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http://dx.doi.org/10.1016/j.jnim.2016.04.005

1. Introduction

Infant development during the last trimester of pregnancy and the first year of life is considered critical for many clinical outcomes like behavior, cognition as well as immunity. During this time of gestation and infancy, there is a large demand for n-3 polyunsaturated fatty acids (n-3 PUFA), like docosahexaenoic acid (DHA), as well as the n-6 PUFA arachidonic acid (AA) [1]. Several scientific and clinical studies show a deficiency in n-3 PUFA negatively impacts physiological outcomes in infants including visual development [2], behavior [3], and cognition [4]. Indeed, numerous studies have found positive correlations between n-3 PUFA consumption and cognition or visual outcomes, although randomized controlled clinical trials are not conclusive [5]. In addition, several studies have linked fish consumption, rich in n-3 PUFA, with infant anthropometric measures [6–8] although the long term biological effect of this is unknown. DHA has also been proposed to exert a suppressive effect in cardiovascular [9] and other chronic inflammatory-related diseases [10] suggesting that DHA modulates immunity. Accordingly, n-3 PUFA intake, in particular DHA, has been expected to provide beneficial effects on infant health and development.

Dietary lipid intake during the pre and post-natal period alters the biochemistry and physiology of the developing infant. Lipids are supplied to infants through placental transfer and breastmilk [1] and a mother's diet influences breastmilk lipid composition [11]. Indeed, DHA in breastmilk is lower in mothers who do not supplement [12]. Similarly, term infants fed standard formula, not fortified with n-3 PUFAs, have lower DHA and AA in their erythrocytes [13] and lower n-3 PUFAs in their cerebral cortex than breastfed infants. Yet, previous meta-analyses on breastfed infants supplemented with n-3 PUFA [14] and fortified formula [15] conclude that n-3 PUFA supplementation cannot be supported or refuted in infants. Still, the American Pregnancy Association recommends 300 mg of DHA daily supplements to pregnant mothers since DHA is deemed essential for neurological and visual development in infants [16] with similar claims made by several infant formula manufacturers.

The aim of this study, was to update previous meta-analyses thoroughly evaluating all clinical trials assessing the effects of n-3 PUFA supplementation, taken maternally or through formula/directly, on infant health and development. Our selection criteria identified 32 infant formula/directly supplemented and 37 breastmilk studies providing data on 2443 infants on n-3 PUFA supplemented formula/direct and 4553 infants feeding from mothers supplemented with n-3 PUFA. This meta-analysis shows that n-3 PUFA supplementation in infants, delivered either maternally or in formula/directly, does not improve visual acuity, language development, or cognition. However, some aspects of growth, motor development, behavior and cardiovascular health are differentially altered in the summary effects with the more desired effect occurring often in breastfed infants compared to formula fed infants. Moreover, this meta-analysis suggests that n-3 PUFA supplementation may affect infant immune development reducing normal pro-inflammatory responses in both breastfed and formula fed infants. Overall, the evidence does not support the continued