

Is There Any Benefit of Supplementing Infant Milk Formulae With Long Chain Polyunsaturated Fatty Acids?

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Simmer K, Patole S, Rao SC. Longchain polyunsaturated fatty acid supplementation in infants born at term. *Cochrane Database of Systematic Reviews* 2008; 1: CD000376. First published online: 23 January 2008.

Simmer K, Schulzke S, Patole S. Longchain polyunsaturated fatty acid supplementation in preterm infants. *Cochrane Database of Systematic Reviews* 2008; 1: CD000375. First published online: 23 January 2008.

Long chain polyunsaturated fatty acids (LCPUFA) such as docosahexaenoic acid (DHA) and arachidonic acid (AA) are considered important in infant nutrition because of their relative abundance in breastmilk, and their role in the structure of cell membranes, particularly those of the central nervous system and retina. Standard milk formulae contain only precursor amino acids from which they have to synthesize their own DHA and AA. Over the last few years, some manufacturers added LCPUFA to infant formulae and started marketing them as advantageous for infant development. These systematic reviews were conducted to assess the effect of providing supplemental LCPUFA in formulae for term and preterm infants, on their growth and neurodevelopment.

SUMMARY

Term Infants

Fourteen randomized controlled trials (RCTs) enrolling 1719 children fed with milk formula enriched with DHA plus AA or DHA alone compared to standard milk formula were included for this review. The sources of LCPUFA included fish oil, egg triglycerides, vegetable oils or fungal oils. The duration of use of the study formula ranged from 2 months to 1 year. The outcomes assessed included visual acuity (as measured by using visual evoked potential or visual acuity cards),

neurodevelopmental outcome (as measured by development scales), and physical growth. Nine studies evaluating effect of supplementation with LCPUFA on visual acuity had inconsistent results with most reporting no benefit at various ages throughout the first three years of life. Pooled meta-analysis of the data from eight studies did not show any statistically significant benefit of LCPUFA supplementation on either mental or psychomotor developmental index of Bayley scale of infant development (BSID) at various ages throughout first two years. Individual studies evaluating other developmental scores had inconsistent results which could not be meta-analyzed because of heterogeneity. Twelve studies evaluated effect on physical growth (weight, length and head circumference) at various ages throughout first three years; none found any benefit or harm of LCPUFA supplementation. The authors concluded that routine supplementation of milk formulae with LCPUFA to improve the physical, neurodevelopmental or visual outcomes of infants born at term can not be recommended based on the current evidence.

Preterm Infants

Fifteen RCTs evaluating the effect of LCPUFA supplemented formulae in enterally-fed preterm (<37 weeks gestation) infants, were included for this review. Meta-analysis of BSID of four studies at 12

KEY MESSAGE

- Supplementation of milk formulae with LCPUFA does not improve the physical, neurodevelopmental or visual outcomes of term or preterm infants.

months ($n = 364$) and three studies at 18 months ($n = 494$) post-term showed no significant effect of supplementation on neurodevelopment. Meta-analysis of five studies showed increased weight and length at two months post-term in supplemented infants. However, meta-analysis of four studies at 12 months ($n = 271$) and two studies at 18 months ($n = 396$) post-term showed no significant effect of supplementation on weight, length or head circumference. The authors concluded that there is no evidence of any benefit or harm of supplementation of formula with n-3 and n-6 LCPUFA on visual development, growth or neurodevelopment of preterm infants.

COMMENTARY***Are the Results Valid and Clinically Important?***

These reviews address some sensible and specific questions. The literature search is comprehensive and most included studies were sound in methods. Although, the functional importance of some of the outcomes such as visual evoked potentials is questionable, more important outcomes of growth and neurodevelopment have been dealt well in these reviews. There was heterogeneity in terms of type and duration of supplementation, the outcome measurement tools, and timing of assessment. Despite this, the authors could formally meta-analyze the results for many important outcomes because of the availability of large number of relevant trials. In the review including term infants, the authors have separately analyzed the results for supplementation with DHA alone or with DHA plus AA. It would have been better if the combined results for any LCPUFA supplementation were

available for these infants as has been done for the review paper on preterm infants.

Implications for Practice and Policy

These systematic reviews provide sound evidence that there is no consistent benefit of supplementing formula with LCPUFA on visual acuity, neurodevelopmental outcomes and physical growth in term or preterm infants. LCPUFA are also considered to be important for development of immune function in the infants(1). The present reviews do not address this issue and it would be interesting to study the effect of LCPUFA supplementation on neonatal/infant infectious morbidities and mortality.

Despite the lack of evidence of benefit from randomized controlled trials, manufacturers are likely to continue adding LCPUFA to formula milks used for preterm and term infants. This is because of the fact that LCPUFA are present in breastmilk and the formula milk companies shall do every effort to match the components with the best in the market *i.e.* breastmilk. The supplemented formulae fetch much more profit for the manufacturers because of their high cost. Unfortunately, the infant food manufacturers of the world are not always driven by evidence!

Funding: None.

Competing interests: None stated.

REFERENCES

1. Yaqoob P, Calder PC. Fatty acids and immune function: new insights into mechanisms. *Br J Nutr* 2007; 98 (Suppl 1): S41-S45.