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COMMENTARY

EBNEO commentary: Maternal high-dose DHA supplementation and neurodevelopment in infants born before 29 weeks' gestation

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This was a planned follow-up study of the Canadian multicentre, randomised, double-blind, placebo-controlled superiority trial, Maternal Omega-3 Supplementation to Reduce Bronchopulmonary Dysplasia in Very Preterm Infants (MOBYDIck). Enrolment in the primary study occurred from 2015 to 2018. A total of 457 infants were included in the final analysis.[1,2] At 18–22 months' corrected age, neurodevelopmental outcomes as assessed by Bayley-III cognitive, language, and motor composite scores were not statistically significant between the treatment and placebo groups.[1] The rates of death before 18–22 months' corrected age, cerebral palsy, hearing impairment and visual impairment were also not statistically significant between the two groups.[1]

Some aspects may bias study results towards the null. First, approximately half the infants in both groups received intravenous

Abbreviations: CI, Confidence interval; DHA, Docosahexaenoic acid; LCPUFA, Long-chain polyunsaturated fatty acid; IVH, intraventricular haemorrhage.

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docosahexaenoic acid (DHA). This was on average for 21–23 days, in the form of DHA-rich lipids. Second, there may have been additional enteral DHA supplementation in both groups. At 6 weeks postmenstrual age, infants received a median of 130–133 mL/kg/day of expressed breast milk.[1] This suggests that many infants at this age were receiving supplemental nutrition, such as donor breast milk or formula. Formula frequently contains DHA.[3] The use of fortifier, which also contains DHA, was not commented on.[4]

The total fatty acid levels in breast milk at 14 days post-delivery were, on average, similar between the groups. In the treatment group DHA composed on average 0.97% of total fatty acids in breast milk at 14 days post-delivery, and in the placebo group, 0.35%.[1] The authors note the hypothesis that sole DHA supplementation may cause an imbalance between the long-chain polyunsaturated fatty acids (LCPUFAs), potentially negating the benefits of high-dose DHA supplementation.[1] Indeed, expert consensus statements recommend that preterm infants are supplemented with multiple LCPUFAs, such as DHA and arachidonic acid.[4,5]

Due to the lower frequency of severe intraventricular haemorrhage (IVH) in the DHA group, a post hoc sensitivity analysis excluding participants with severe IVH was completed. This did not change the primary findings. Subgroup analysis found that for neonates born <27 weeks' gestation, those in the treatment group had a higher language score (mean difference 5.06, 95% CI 0.08–10.03; $p = 0.05$). This analysis was not adjusted for the imbalance in frequency of IVH.[1]

Further study limitations are well documented by the authors. This includes a suboptimal sample size limiting study interpretation, as enrolment for the MOBYDIck trial was terminated early due to concern that DHA was associated with bronchopulmonary dysplasia.[1] Additionally, the sample size was chosen for the primary outcome of the MOBYDIck trial, and therefore has limited ability to detect differences in the primary outcome of this study.

Despite the theoretical benefit of LCPUFA supplementation for preterm infants, several randomised controlled trials and a Cochrane systematic review have found little, if any, clinical neurodevelopmental effect.[4,6,7,8,9] This study is important as there is limited data on very preterm and extremely preterm infants. Based on this trial, maternal supplementation with high-dose DHA in breastfed infants born before 29 weeks' gestational age does not improve neurodevelopmental outcomes at 18–22 months' corrected age.

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AUTHOR CONTRIBUTIONS

DV wrote the initial draft with AK providing key input. All authors revised the paper for critical scientific content.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

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