

DHA in Neonates

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Expanded Commentary from the Faculty

We've known for about 2 decades that some long-chain polyunsaturated fatty acids (LCPUFAs) such as docosahexaenoic acid (DHA) are critical for brain and retinal function in infants, and we are now learning more about LCPUFAs' ability to regulate immunity and the potential to affect morbidity in other organs.

During the third trimester of pregnancy, the mother transfers DHA and other LCPUFAs to the fetus. In premature infants, this transfer is cut short, putting them at risk for LCPUFA deficiency, which is associated with developmental, neurologic, respiratory, and infectious consequences.

In a randomized trial of 657 premature infants (<33 weeks' gestation) called the DINO (Docosahexaenoic Acid for the Improvement of Neurodevelopmental Outcomes in Preterm Infants) Trial, Manley et al reported on pulmonary outcomes with oral DHA supplementation. These researchers gave breastfeeding mothers either tuna-oil supplements containing high levels of DHA or soy-oil supplements containing a standard amount of DHA. Both groups continued on the supplements for about 9 weeks. The results showed that babies who received the high-level DHA via their mother's breast milk had less respiratory morbidity at 36 weeks. This was especially apparent among the smallest babies, those weighing <1250 grams, who tend to suffer from the most respiratory disease. So this is a pretty significant outcome and compelling evidence that we need to provide adequate DHA and continue to provide it for several weeks of life.

There are some recent data from Robinson et al and Martin et al showing that levels of LCPUFAs drop quite dramatically in premature infants within several weeks of their birth. Although breast milk and premature infant formulas contain varying amounts of DHA and other LCPUFAs, very premature infants are often not receiving this form of nutrition. Instead, they typically receive Intravenous (IV) fat emulsions for the first few weeks of life, which unfortunately don't contain DHA (at least in the United States; such products are available in South America, Australia, and Europe). In fact, the Robinson study found that very-low-birth-weight infants who received an IV lipid emulsion (without DHA) for >28 days actually had lower DHA levels than babies who received the fat emulsion (again, without DHA) for ≤28 days.

Unfortunately, as I mentioned, we don't have a Food and Drug Administration (FDA)-approved IV DHA product available in the United States. Although IV DHA supplements have been shown to be safe, well-tolerated, and efficacious in international studies, the FDA wants to see data from large randomized clinical trials of these products conducted here and these trials are very costly. It's ironic that we have one of the largest populations of preterm babies in the world,

and other areas of the world have an IV DHA preparation and we don't. So I would love to see the neonatology community rally to convince the FDA to okay an IV lipid solution that provides DHA. I'd also like to see more data on giving DHA supplements to breastfeeding mothers. It can be difficult to convince breastfeeding mothers to take high-dose DHA supplements and we need to identify the best preparations to use, so I hope that OB/GYNs will get involved in this practice, because they have access to moms.

The bottom line is that we invest an enormous amount of money in saving premature infants, but they have a lot of morbidity, including chronic lung disease. If we can intervene by offering them better nutrition with DHA supplementation, they will grow better over the short term and have less morbidity and better long-term outcomes.

Group Discussion Items

- How much has DHA been on your 'radar'?
- Do you see this as a problem or critical issue?
- Does the commentary provided by Dr. Moya align with our current practice? In what ways?
- Without an FDA-approved IV DHA product available to us in the United States, how do we approach this problem/issue?
- Has anyone had a conversation with a mom that discussed DHA supplementation?
- What is our current practice of informing mothers about DHA supplementation? Why is it the way it is?
- What other approaches or resources could be used?
- Are there other internal or hospital barriers not addressed here?

Suggested Readings and Resources

1. Manley BJ, Makrides M, Collins CT, McPhee AJ, et al. **High-dose docosahexaenoic acid supplementation of preterm infants: Respiratory and allergy outcomes.** *Pediatrics*. 2011;128:e71-e76.
2. Robinson DT, Carlson SE, Murthy K, Frost B, et al. **Docosahexaenoic and arachidonic acid levels in extremely low birth weight infants with prolonged exposure to intravenous lipids.** *J Pediatr*. 2013;162:56-61.

3. Martin CR, Dasilva DA, Cluette-Brown JE, Dimonda C, et al. **Decreased postnatal docosahexaenoic and arachidonic acid blood levels in premature infants are associated with neonatal morbidities.** *J Pediatr.* 2011;159:743-749.
4. Bernardi JR, Escobar RD, Ferreira CF, Silveira PP. **Fetal and neonatal levels of omega-3: Effects on neurodevelopment, nutrition, and growth.** *Sci World J.* 2012;article id 202473; doi:10.1100/2012/202473.
5. Lapillone A, Groh-Wargo S, Gonzalez CH, Uauy R. **Lipid needs of preterm infants: Updated recommendations.** *J Pediatr.* 2013;162(3 Suppl):S37-S47.