Preterm Infants Given Fish Oil Emulsions May Have Less Retinopathy of Prematurity

Preterm infants born before 36 weeks’ gestation or those born weighing less than 1,250 grams are at high risk of mortality and morbidity, with risk increasing as gestational age decreases. Recently published findings from the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network on the mortality and morbidity of nearly 10,000 infants of extremely low gestational age and birthweight describe the high rates of illness among the survivors. Early nutritional support reduces the severity of illness in these infants, though attention to LC-PUFAs has only recently been included. The leading illnesses in very low birthweight preterm infants are respiratory distress syndrome (93%), bronchopulmonary dysplasia (supplemental oxygen use at 36 weeks postmenstrual age) (68%), retinopathy of prematurity (59%), patent ductus arteriosus (46%), late-onset sepsis (36%), severe intraventricular hemorrhage (16%), necrotizing enterocolitis (11%) plus others.

Retinopathy of prematurity (ROP) results from the abnormal development of blood vessels in the retina, which begin to grow 3 months after conception. Long-chain omega-3 PUFAs (n-3 LC-PUFAs) are also required for the healthy development of visual function and have been shown to reduce the area of vascular damage and increase healthy vessel regrowth in ROP and similar diseases. Eventually, the outer rods of the photoreceptors in the retina achieve the highest concentration of DHA in the body. In early pregnancy, ARA is
highly concentrated in the endothelial cells lining the vascular system of the placenta and is necessary for healthy vascularization. Thus, DHA and ARA appear to be critical for reducing the risk and severity of the condition.

Preterm infants are born with lower LC-PUFA status than term infants because these fatty acids are predominantly transferred from the mother in the third trimester. The shortfall in LC-PUFAs, especially of DHA, may be exacerbated by the provision of soybean emulsions devoid of LC-PUFAs immediately after birth and the low rates of conversion of alpha-linolenic acid in soybean oil to long-chain omega-3 PUFAs (n-3 LC-PUFAs). Lipid emulsions containing a mixture of soybean and fish oils with other lipids increased the concentration of n-3 PUFAs in preterm infants, reversed parenteral nutrition-associated liver disease in infants and were reported safe and effective in adult abdominal surgery patients. In a recent study of preterm infants weighing <1,250 g, a fish oil lipid emulsion significantly increased plasma and red blood cell phospholipid DHA and EPA and reduced ARA concentrations. The use of combined fish and soybean oils in preterm infant emulsions improves LC-PUFA status and appears safe and effective.

In this study, 40 preterm infants weighing <1,250 g were treated with a parenteral nutrition emulsion consisting of 50% soybean/olive oil and 50% fish oil supplied as 10% Omegaven® containing 1.4 – 3.1 g/mL of DHA, 1.3 – 2.8 g/mL of EPA and 0.1 – 0.4 g/mL of ARA. For comparison purposes, the demographic and clinical results were compared with an historical cohort of 44 preterm infants weighing <1,250 g, with a similar median gestational age of 28 weeks. The historical cohort received only the soybean/olive oil emulsion. Both groups received the lipid emulsions from the first day of life as a continuous 24-hour infusion. The
The initial daily dose was 0.5 g of lipid per kg body weight for infants weighing <1,000 g and 1.0 g/kg body weight for infants >1,000 g. The lipid emulsions were increased by 0.5 or 1.0 g of lipid per kg body weight every 24 hours to a maximum of 3.0 to 3.5 g per kg body weight per day.

Infants receiving enteral nutrition were given breast milk or n-3 LC-PUFA-enriched neonatal formula, with 87% and 91% of the experimental and historical groups, respectively, receiving their own mother’s breast milk. Enteral feeding gradually replaced total parenteral nutrition to maintain the total lipid dose at 3.0 to 3.5 g of lipids/kg body weight daily. Primary outcomes of the study were development of ROP, need for photocoagulation therapy and the occurrence of cholestasis defined as a direct bilirubin value >1.0 mg/dL if the total bilirubin level was < 5 mg/dL. The investigators screened for ROP from the third to fourth week of life, continuing every second week thereafter. When ROP was diagnosed, evaluations continued weekly in both ROP and control infants. Visual acuity and functional integrity of the visual pathways in all infants who developed any stage of ROP were evaluated at 18 and 24 months’ corrected age.

There were no significant differences in mortality between the 2 groups, with 25.3% mortality in the fish oil group and 27.9% in the historical group. Cholestasis did not occur in the fish oil infants, but was diagnosed in 5 of the 44 control infants. ROP occurred at similar rates in the 2 groups (32.5% in the fish oil group, 36.3% in the control group), but the outcomes differed substantially. Ten of the 13 ROP infants fed the fish oil emulsion experienced a spontaneous regression of the condition and 3 required laser therapy. In the control group, 12 of 16 infants with ROP received laser therapy, a significant difference in treatment interventions ($P = 0.023$). Of the 29 infants who developed
ROP, 26 had visual acuity assessments and 22 were within the normal range.

The main finding from this observational study was a significantly lower risk of laser treatment for ROP in infants who received the fish oil emulsion immediately after birth. Ten of the 13 infants with ROP who consumed the fish oil emulsion had their condition resolve spontaneously without therapy. In contrast, 12 of the 16 infants with ROP in the control group required laser therapy. These observations need to be confirmed in a randomized controlled trial. However, the study is consistent with the need for DHA in the development of the retina and the shortfalls in LC-PUFAs observed in preterm infants born below 1,250 grams. The implication is that the immediate provision of n-3 LC-PUFAs after preterm birth might reduce the risk of developing severe ROP and possibly other illnesses associated with preterm birth.