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Marine Oils

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Drug Levels and Effects

Summary of Use during Lactation

Marine oils, such as fish oil or algal oil, are a rich source of omega-3 fatty acids, especially the essential fatty acids, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). Algal oil is high in DHA and low in EPA, whereas fish oil has more EPA than DHA. DHA and EPA are normal components of breastmilk in which concentrations reflect maternal intake. The DHA level in breastmilk is typically between 0.2% and 0.3% in Western countries.[1] This is usually sufficient to meet the DHA requirements of term breastfed infants, but not the higher requirements of pre-term infants, where additional maternal supplementation is needed.[2] Maternal supplementation increases breastmilk levels of DHA and EPA, although it appears that milk concentrations depend more on long-term intake than short-term (past 3-days) intake.[3,4] Higher milk levels result in higher infant plasma and erythrocyte levels of omega-3 fatty acid-derived phospholipid; one study found that breastmilk DHA was a better predictor of infant erythrocyte DHA than direct supplementation of the infants with fish oil.[5] Current dietary recommendations for nursing mothers is 250 to 375 mg daily of DHA plus EPA.[6] Lactating women require a daily dosage of about 1000 mg DHA plus EPA to reach a milk DHA plus EPA of 1 g/dL at 4 weeks postpartum.[7]

Supplementation with omega-3 fatty acids has been studied for reduction of postpartum depression in nursing mothers and for improving various infant outcomes. A meta-analysis of 35 randomized, controlled trials found that women with a diagnosis of severe depression obtained benefit from omega-3 fatty acids, but those with mild depression did not.[8]

A meta-analysis of randomized, controlled trials on infant neurodevelopmental outcomes found that maternal supplementation with essential fatty acids during pregnancy and breastfeeding for the first 4 months postpartum did not improve the child's problem solving ability, intelligence, or psychomotor or motor development. Weak evidence for improved vision and attention was found in one study.[9] Two meta-analyses found that maternal supplementation with omega-3-polyunsaturated fatty acids during lactation had little or no beneficial effect on childhood allergic diseases.[10,11] Another meta-analysis using different selection criteria found that supplementation of the mother with omega-3-fatty acids during pregnancy and/or breastfeeding had no beneficial effect on visual acuity, growth or language development. Some aspects of motor, cardiovascular health, behavior and immunity were found to be differentially affected by supplementation, with the more desired effect

occurring more often in breastfed infants than in formula-fed infants.[12] One subsequent study found fewer allergies in the breastfed infants of supplemented mothers, but could not distinguish between supplementation during pregnancy and during breastfeeding.[13] Another study that gave fish oil to women during pregnancy and lactation found no clear benefit or harm of fish oil supplementation on children's neurodevelopment at 5 years of age.[14] Long-term follow-up of a small group of children whose mothers received fish oil supplements during lactation found that boys had a delayed puberty, shorter average height, and higher systolic blood pressure at age 13 years.[15] Another study found that maternal fish oil supplementation during pregnancy and lactation reduced oxidative stress in their breastfed infants.[16]

Fish oil up to 3 grams daily is "generally recognized as safe" (GRAS) as a food by the U.S. Food and Drug Administration. The most common complaint is burping a fishy taste after ingestion. However, breast milk odor is not changed by maternal fish oil consumption.[17] Rarely, allergic reactions are reported with nut oil-derived omega-3 fatty acids in patients allergic to nuts.

Dietary supplements do not require extensive pre-marketing approval from the U.S. Food and Drug Administration. Manufacturers are responsible to ensure the safety, but do not need to *prove* the safety and effectiveness of dietary supplements before they are marketed. Dietary supplements may contain multiple ingredients, and differences are often found between labeled and actual ingredients or their amounts. A manufacturer may contract with an independent organization to verify the quality of a product or its ingredients, but that does *not* certify the safety or effectiveness of a product. Because of the above issues, clinical testing results on one product may not be applicable to other products. More detailed information about dietary supplements is available elsewhere on the LactMed Web site.

Drug Levels

Numerous studies have examined the effect of omega-3 fatty acid ingestion during pregnancy and lactation on breastmilk fatty acid composition. Only studies in which supplementation was started postpartum are reviewed below.

Maternal Levels. Five nursing mothers were supplemented with fish oil containing 1080 mg of EPA and 720 mg of DHA daily for 21 days, beginning at 2 weeks postpartum. Milk samples were collected daily before the dose; once weekly, milk samples were also collected at 4, 8, 12 and 16 hours after the dose. On day 21, predose milk levels of DHA (by 89%), EPA (by 525%) and another omega-3 fatty acid (docosapentaenoic acid; by 143%) were significantly increased over their initial levels. Mean and peak levels increased each week during the study on each of the days were sequential levels were measured. Peak omega-3 fatty acid levels occurred 12 hours after ingestion.[18]

New mothers intending to breastfeed for at least 12 weeks were randomized to receive placebo (n = 12) or algal-derived DHA in a dose of 0.2 (n = 10), 0.4 (n = 12), 0.9 (n = 10) or 1.3 (n = 8) grams daily starting at day 5 postpartum. At 12 weeks postpartum, DHA levels in breastmilk were linearly proportional to the dose of DHA ingested, expressed as the following percentages of total breastmilk fatty acids: 0.21% (placebo), 0.35% (0.2 grams), 0.46% (0.4 grams), 0.86% (0.9 grams), and 1.13% (1.3 grams).[19]

Mothers who were breastfeeding at least 75% were randomized to receive supplements of either high-DHA algal oil (n = 6), high-DHA eggs (n = 6), low EPA fish oil (n = 6) or regular eggs (n = 6) beginning at 2 weeks postpartum. Supplementation provided doses of < 230 mg, 170 mg, 260 mg and <35 mg daily of DHA, respectively. After 6 weeks of supplementation, breastmilk DHA was increased in all supplemented groups and correlated with DHA intake. Breastmilk DHA was decreased in the regular egg group.[20]

Ten mothers of preterm infants (<29 weeks gestational age) were given 1200 mg of DHA daily beginning within the first week postpartum and continued for 8 to 12 weeks. A group of 22 mothers who met the same criteria, but without maternal supplementation served as a reference group. The average DHA breastmilk concentration

in supplemented mothers increased 5-fold over the baseline value within the first week of supplementation. Breastmilk DHA in the supplemented group was about 12 times higher than in the reference group at 49 days postpartum.[21]

A double-blind study randomized 51 mothers of newborn, term infants to receive normal diet (control), normal diet plus 224 mg daily of DHA from algal oil, or normal diet plus 150 grams of fatty fish 3 times weekly. Supplemented mothers maintained consistent DHA levels in colostrum, transitional and mature milk. Mothers on normal diets had a decrease in DHA from colostrum to mature milk. The amount in mature milk was significantly less than that in the milk of supplemented mothers.[22]

Mothers who donated milk to a milk bank were randomized to receive either single-cell algal oil capsules equivalent to 1 gram of DHA (n = 6), daily or placebo capsules (n = 7). Mothers in both groups had DHA intake lower than recommended at baseline. The DHA content of milk increased in supplemented mothers. The milk of supplemented mothers provided a sufficient amount of DHA for preterm infant, but not the milk of unsupplemented mothers.[23]

Eighty-two nursing mothers who were 4 to 6 weeks postpartum were randomly assigned to take placebo, 200 mg or 800 mg DHA supplements daily each morning with food for 6 weeks. Mothers supplied a mid-nursing breastmilk sample before starting the supplementation and once weekly for 6 weeks. Compared to mothers who received a placebo, breastmilk levels of DHA were 50% higher for mothers who took 200 mg of DHA daily and 123% higher for mothers who took 800 mg DHA daily.[24]

One hundred ten mothers were randomly assigned to receive either a control drink (n = 54) or a drink (n = 56) containing fish oil with 72 mg of EPA and 320 mg/dL of DHA daily in two doses during pregnancy and lactation. Breastmilk samples were obtained at birth (colostrum) and at the first second and fourth month postpartum. The content of DHA and EPA as well as n-3-polyunsaturated fats were higher in the milk of supplemented mothers at all time points.[25]

Ninety-five pregnant women at risk of having an allergic infant were randomized to daily supplements of 2.7 grams of omega-3 fatty acids (EPA 1.6 grams and DHA 1.1 grams) or a placebo from week 25 of pregnancy until 3 months of lactation. Breast milk samples were collected as colostrum, and at one and 3 months postpartum. Omega-3 milk fatty acids were higher in women who received omega-3 supplements than in the placebo group at all time points.[13]

Eight women received a fish- and krill-oil supplement (Krilling D, Italchimici S.P.A.,Milan, Italy) in a dose of 250 mg of DHA and 70 mg of EPA daily for 30 days. A control group of 8 women did not receive the supplement. Five of the 8 women who received the active drug had abnormally low intake of DHA than recommended by guidelines at the beginning of the study. Both DHA and EPA milk levels were higher at the end of 30 days in the supplement group than in the control group.[26]

Infant Levels. Five nursing mothers were supplemented with fish oil containing 1080 mg of EPA and 720 mg of DHA daily for 21 days, beginning at 2 weeks postpartum. The infants' average erythrocyte content of EPA increased by 636% and docosapentaenoic acid increased by 260% on day 21 compared to baseline. The ratio of omega-6 to omega-3 fatty acids decreased significantly by 22%. DHA content was increased only slightly, but the difference was not statistically significant.[18]

New mothers intending to breastfeed for at least 12 weeks were randomized to receive placebo (n = 12) or algal-derived DHA in a dose of 0.2 (n = 10), 0.4 (n = 12), 0.9 (n = 10) or 1.3 (n = 8) grams daily starting at day 5 postpartum. At 12 weeks, their breastfed infants had blood samples measured for plasma and erythrocyte DHA-derived phospholipid. The DHA-phospholipid levels increased proportionately up to a milk DHA level of about 0.8% of total milk lipids, then reached a plateau where higher milk DHA concentrations did not further increase

infant DHA-phospholipid levels. Infant EPA-phospholipid levels also increase slightly, while omega-6 fatty acid phospholipids decreased.[27]

Mothers who were breastfeeding at least 75% were randomized to receive supplements of either high-DHA algal oil (n = 6), high-DHA eggs (n = 6), low EPA fish oil (n = 6) or regular eggs (n = 6) beginning at 2 weeks postpartum. Supplementation provided doses of < 230 mg, 170 mg, 260 mg and <35 mg daily of DHA, respectively. After 6 weeks of supplementation, infant plasma DHA-phospholipid was increased in all supplemented groups, with the highest in the alga oil group. DHA increased only slightly in the regular egg group.[20]

Ten mothers of preterm infants (<29 weeks gestational age) were given 1200 mg of DHA daily beginning within the first week postpartum and continued for 8 to 12 weeks. A group of 22 mothers who met the same criteria, but without maternal supplementation served as a reference group. Infants were exclusively fed their mother's breastmilk if possible, but some were partially formula fed. At 49 days of age, the infants whose mothers were given DHA supplementation received an estimated 55 mg/kg daily of DHA and the reference group infants received 7 mg/kg daily of DHA.[21]

Eighty-two nursing mothers who were 4 to 6 weeks postpartum were randomly assigned to take placebo, 200 mg or 800 mg DHA supplements daily each morning with food for 6 weeks. After 6 weeks of supplementation of their mothers, breastfed infants' plasma DHA increased by 71% and 101% for the infants of low- and high-dose supplements, respectively, compared to the placebo group. The plasma omega 6:3 ratios were lower in the infants of supplemented mothers.[24]

One hundred ten mothers were randomly assigned to receive either a control drink (n = 54) or a drink (n = 56) containing fish oil with 72 mg of EPA and 320 mg/dL of DHA daily in two doses during pregnancy and lactation. Infants were breastfed, but the extent was not stated. At 2.5 months of life, DHA, n–3 and C24:1 –9 polyunsaturated fatty acids were higher in the plasma and erythrocyte membranes of the infants of supplemented mothers. EPA levels were also higher in the plasma of the infants whose mothers were supplemented.[25]

Effects in Breastfed Infants

Ninety-five pregnant women at risk of having an allergic infant were randomized to daily supplements of 2.7 grams of omega-3 fatty acids (EPA 1.6 grams and DHA 1.1 grams) or a placebo from week 25 of pregnancy until 3 months of lactation. Infants of supplemented mothers had fewer allergies than unsupplemented infants, but it is unclear is the results were caused by transfer during pregnancy or during lactation.[13,28]

A small sample of children whose mothers were randomized to receive either fish oil or olive oil during the first 4 months of lactation were examined at 13 years of age. Boys, but not girls, whose mothers received fish oil supplements trended towards short heights, apparently because of a delay in puberty. Boys also had a statistically significantly higher systolic blood pressure by an average of 3.9 mm Hg than girls.[15]

One study found that supplementation of mothers with fish oil during pregnancy and postpartum lactation decreased plasma hydroperoxides especially in newborn at delivery and at 2.5 months of age and increased superoxide dismutase and catalase in breastfed infants newborns at 2.5 months of age. All of these changes indicate a decrease in oxidative stress in the infants.[16]

Fifty-two breastfeeding mothers provided milk samples at 3 months postpartum for fatty acid analysis and completed the Infant Behavior Questionnaire. Infants whose mothers' milk was richer in n-3 PUFAs had lower scores on the negative affectivity domain of the IBQ-R, a component of temperament associated with a risk for internalizing disorders later in life. These associations remained statistically significant after considering

covariates, including maternal age, marital status, and infant birth weight. The n-6 PUFAs, n-6/n-3 ratio, and total fat of milk were not associated with infant temperament.[29]

Effects on Lactation and Breastmilk

Relevant published information was not found as of the revision date.

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Substance Identification

Substance Name

Marine Oils

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8016-13-5

Drug Class

Breast Feeding

Lactation

Complementary Therapies

Food

Oils

Phytotherapy

Plants, Medicinal