Wyoming Drug Utilization Review

Omega-3s in Pregnancy

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What are Omega-3s?

Omega-3 fatty acids, otherwise known as long-chain omega-3 polyunsaturated fatty acids, are essential nutrients. Essential nutrients must be obtained in the diet since our bodies are unable to synthesize them.[1] Two omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are of great importance because they are the most biologically active forms of omega-3s. In the body, alpha-linolenic acid (ALA) is converted to EPA, which is then converted to DHA. This process is inefficient and therefore omega-3s need to be consumed in the diet.[1]

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The Role of Omega-3s in Pregnancy

DHA and EPA are necessary for normal neuronal and visual development in the fetus.[3] DHA collects in fetal tissue rapidly during the third trimester of pregnancy.[4] Therefore, it is important that the level of omega-3 fatty acids in the mother is sufficient at this time to provide a source of these nutrients to the fetus.[3] It is reported that DHA deficiency "leads to reduced dendritic arborization and impaired gene expression for regulation of neurogenesis, neurotransmission, and connectivity."[5]

Not all of the benefits of omega-3 fatty acids in pregnancy are fully understood. Studies examining the possible benefits of omega-3s in pregnancy have conflicting results.[1] Currently, researchers are investigating the ability of omega-3s, when supplemented in pregnancy, to decrease allergies in infants, increase length of gestation, decrease risk of preterm labor, enhance cognitive development, and prevent and treat perinatal depression. Because omega-3 fatty acids are necessary for neuronal and visual development and may have other benefits, guidelines recommend at least 200 mg of DHA per day for pregnant women.[1]

Omega-3s and Allergic Disease in Infants

Possible Mechanism of Action: DHA and EPA show immunomodulatory properties. The omega-3 fatty acid may "mitigate the severity of the allergic phenotype, possibly through preventing allergic sensitization."[2]

The Evidence: Furuhjelm et al. examined the effects of omega-3 supplementation in pregnancy and lactation in the first two years of life in terms of IgE-associated diseases and the frequency and severity of allergic disease in infants.[2] Pregnant patients with high risk of allergy in their families were randomized to receive either 1.6 g EPA and 1.1 g DHA daily or placebo. Supplementation began at 25 weeks gestation and continued through 3.5 months of breastfeeding. The point prevalence of allergic symptoms at 24 months in infants did not differ between the two groups; however, the incidence of any IgE-associated disease was significantly lower in the supplemented group. The incidences of IgE-associated eczema and Ig-E-mediated food reactions, specifically, were significantly decreased in the supplemented group.[2]

The finding of a difference in the incidence but not prevalence of IgE-mediated diseases between the two groups could be explained by infants growing out of allergies. This study concludes that in pregnant women with high risk of allergy in their families, DHA and EPA supplementation may have a role in decreasing allergic sensitization in infants.[2]

It should be noted that this study extended supplementation beyond pregnancy by several months in breast-feeding women. Additionally, effects beyond the first two years of life were not assessed. The researchers state that the data does not provide information to determine the optimal maternal dose of DHA and EPA to decrease the rate of IgE-associated disease in infants.[2]

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Potential Effects Related to Neurodevelopment
Possible Mechanism of Action: The composition of omega-3 fatty acids is important in maintaining membrane stability of various cells. Omega-3s also have an effect on gene expression as well as tissue differentiation.[3]

The Evidence: Sequential Processing
Helland et al. found women who were supplemented with omega-3s during pregnancy and lactation had children with higher IQ scores at the age of four years.[6] The researchers then re-examined the children in a follow-up study at seven years of age. No difference in IQ was found between the children of mothers who were supplemented and the children of mothers who received placebo. In this follow-up study, researchers did find a correlation between maternal concentrations of ALA and DHA during pregnancy with sequential processing in the seven year olds.[6]

The Evidence: Problem Solving
A benefit in infant ability to problem solve has also been shown in nine month old children whose mothers were supplemented with an average of 1500 mg DHA per week.[4] In this trial, women were randomized to either an active or control group. Women in each group consumed cereal-based bars, but only half the bars contained 300 mg of DHA. The women were instructed to consume up to seven bars per week from gestation week 24 to delivery.[4] Infants were tested at nine months of age to measure intention score and intentional solution score, both findings were significant in favor of the children whose mothers were supplemented with DHA during pregnancy. No difference was found in recognition memory between the two groups.[4]

The Evidence: Hand and Eye Coordination
A positive effect on development of a child's hand and eye coordination has also been reported. Dunstan et al. conducted a randomized, placebo controlled trial in which pregnant women received either placebo or 2.2 g DHA and 1.1 g EPA daily from 20 weeks gestation until delivery.[3] Children were evaluated at 2.5 years of age for development, receptive language, and behavior.[3] Children of mothers who received DHA and EPA scored significantly higher in measurements of hand and eye coordination than children from mothers who received placebo. When statistical analysis was performed accounting for potential confounders, including maternal age, maternal education and duration of breast feeding, the finding was still significant. No difference was found in terms of receptive language or behavior.[3]

The Evidence: IQ, Behavior, and Communication
A cohort study reported that children of mothers who received inadequate levels of omega-3s during pregnancy were more likely to have lower total IQs at the age of eight years, behavior problems at the age of seven years, suboptimal communication skills, and suboptimal fine-motor skills and social skills.[5] Communication skills were measured at six and 18 months. Fine-motor skills were significantly different beginning at 18 months of age and were last measured at 42 months of age. Social skills were significantly different beginning at 30 months of age and were last measured at 42 months of age.[5] Whether these effects carry forward in children beyond 18 and 42 months (depending on the effect in question) is unknown based these studies.

Is the Length of Gestation Related to Omega-3 Status During Pregnancy?
Possible Mechanism of Action: Several randomized, controlled trials have presented varying results regarding the effect of omega-3s on length of gestation.[1] The hypothesized mechanism of action behind preventing preterm birth involves promoting an increased ratio of omega-3 to omega-6 fatty acids in the body. Omega-6 fatty acids are responsible for proinflammatory effects through increased production of prostaglandin E_2 and prostaglandin $F_{2\alpha}$. These proinflammatory eicosanoids have been indicated in preterm labor. Omega-3s, on the other hand, appear to down-regulate prostaglandin production and may promote myometrial relaxation.[1]

The Evidence: Judge et al. found that women supplemented with DHA had a significantly longer gestational period as compared to women who received placebo. This trial involved a small number (29) of participants.[4]

Alternatively, a large randomized placebo-controlled trial examined the effect on gestational length and preterm birth in pregnant women taking 400 mg DHA from gestational week 18 through delivery. Gestational period and rate of preterm birth did not differ between the women who were supplemented and those who received placebo.[7]

Perinatal Depression
Possible Mechanism of Action: Cytokine production has been reported to be elevated in depressed patients. Omega-3s have been shown to down-regulate production of these proinflammatory mediators.[1]

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P & T Committee Meeting Update

The P&T Committee met for its quarterly business meeting on August 30, 2012. Highlights of this meeting include:

The following prior authorization was approved:

Oxycodone immediate release products will be limited to a maximum dose of 90 mg/day. Anything above this amount will require prior authorization.

Prior authorization will be required for concomitant use of Suboxone and opiates, carisoprodol, short-acting benzodiazepines and short-acting stimulants.

Dose limits will be applied to antidepressants and benzodiazepines.

The following changes to prior authorization were approved:

Latuda, Saphris and Fanapt will be preferred agents for the treatment of schizophrenia and bipolar disorder.

Cymbalta will be allowed for use in patients with chronic low back pain.

All proposed prior authorization criteria will be posted for public comment at www.uwyo.edu/DUR. Comments may be sent by email to alewis13@uwyo.edu or by mail to: Wyoming Drug Utilization Review Board, Dept. 3375, 1000 E. University Avenue, Laramie, WY 82071. Comments should be received prior to September 30, 2012.

The next P&T Committee meeting will be held November 15, 2012 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

2013 P&T Committee Meeting Dates

March 7, 2013
May 16, 2013
August 22, 2013
November 21, 2013

Meetings are held in Cheyenne at Laramie County Community College from 9 am - 1 pm.

Omega-3s in Pregnancy, continued

The Evidence: Studies have produced conflicting results. Observational studies have found low seafood intake correlates with depression in pregnancy. Researchers have further investigated this finding in randomized controlled trials, but results have not shown omega-3 consumption during pregnancy improves perinatal depression. This is a difficult topic to study given the many variables that can affect depression and thus cloud study results.[1]

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