Fish Oil Didn’t Help Postpartum Depression

BY MARY ANN MOON
FROM JAMA

The use of DHA-rich fish oil supplements during pregnancy did not reduce the rate of postpartum depression in mothers or improve neurodevelopment in their children, according to a report.

“Current recommendations suggest that pregnant women increase their dietary DHA (docosahexaenoic acid) to improve their health outcomes as well as those of their children,” and the industry “successfully markets prenatal supplements with DHA to optimize brain function of mother and infant,” noted Maria Makrides, Ph.D., of Women’s and Children’s Hospital at Flinders Medical Centre in Adelaide, Australia, and her associates.

However, intervention trials with open-label designs, small sample sizes, high attrition rates, or poor statistical power have produced inconclusive results. Dr. Makrides and her colleagues performed the DOMINO (DHA to Optimize Mother-Infant Outcome) trial to assess the efficacy and safety of DHA supplements.

In the double-blind trial, 2,230 women with singleton pregnancies attending five Australian perinatal centers were randomly assigned to take three fish oil capsules (1,197 women) or placebo capsules containing vegetable oil (1,202 women) daily. The fish oil capsules contained 800 mg/day of DHA and 100 mg/day of eicosapentaenoic acid. The study subjects were enrolled before they reached 21 weeks’ gestation and took the supplements until delivery (JAMA 2011;304:1675-83).

The primary maternal outcome was a high level of depressive symptoms during the first 6 months postpartum, as assessed...
from the pooled dataset. The most common treatment-emergent adverse reactions (2% vs. users: headache (0.9% vs. users: 1.5%), fatigue (0.7% vs. users: 0.4%), menstrual irregularities (0.3% vs. users: 0.1%), and headache (0.2% vs. users: 0.1%).

PMDD Clinical Trials

Safety data from trials for the indication of PMDD are reported separately due to differences in study design and setting in the USA and Europe. The adverse events reported in the PMDD clinical program include:

Common treatment-emergent adverse reactions (2% vs. users: menstrual irregularities (0.4%), urinary tract infection (0.3%), and headache (0.2% vs. users: 0.1%).

Adverse Reactions (1%) Leading to Discontinuation:

In vitro

4HE ADMINISTRATION OF S/TO INDUCE WITHDRAWAL BLEEDING SHOULD NOT BE USED AS A TEST FOR PREGNANCY.

PREGNANCY% PEDIATRIC STUDIES AND META ANALYSES HAVE NOT FOUND AN INCREASED RISK OF GENITAL OR NON-

Several drugs have been reported to reduce folate levels by inhibition of the dihydrofolate reductase (DHFR).

7.5 Effects of Other Drugs on Folates

ACUTE HEART FAILURE, MYOCARDIAL INFARCTION, OR ARRHYTHMIAS MAY REDUCE SEIZURE CONTROL; THEREFORE DOSAGE ADJUSTMENTS OF LAMOTRIGINE MAY BE NECESSARY. CONSULT THE THE THERAPEUTIC USE OF FOLIC ACID PROVIDES THE SAME DAILY VITAMIN REQUIREMENTS AS EVOMEFOLATE CALCIUM.

8.1 Pregnancy

There is a potential for an increase in serum potassium in women taking Beyaz with other drugs that alter potassium metabolism. This is less likely to occur if breastfeeding is well established.

VASCULAR DISORDERS: VENOUS AND ARTERIAL THROMBOEMBOLIC EVENTS (INCLUDING PULMONARY EMBOLI, DEEP VEIN THROMBOSIS, AND PULMONARY HYPERTENSION). INCREASED PLASMA LEVELS POSSIBLY BY INHIBITION OF CONJUGATION INHIBITORS SUCH AS ITRACONAZOLE OR Ritonavir.

67% of women, 9.4% discontinued from the clinical trials due to an adverse reaction; the most frequent adverse reactions leading to discontinuation were headache/migraine (4.6%), nausea/vomiting (4.6%), and headache (1.0%).

Acne Clinical Trials: 6.5% discontinued from the clinical trials due to an adverse reaction; no reaction leading to discontinuation occurred in 7% of women.

PMDD Clinical Trials:

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5.2 Drug Interactions

CONSIDER THE POTENTIAL OF EVOMEFOLATE CALCIUM TO INHIBIT THE METABOLISM OF CYP2C9/19 SUBSTRATES SUCH AS OXCARBAZEPINE AND LAMOTRIGINE.

7 DRUG INTERACTIONS

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5.2 Drug Interactions

6.4 Pediatric Use

6.5 Pregnancy

5.4 Precautions

These findings are based on the analysis of data from clinical trials and postmarketing experience. The administration of the COCs to reduce withdrawal bleeding should not be used as a test for pregnancy. COCs should not be used during breastfeeding.

5.4 Precautions

The women who took fish oil supplements had a lower rate of very preterm birth (1.1%) compared with the control group (2.9%). This finding was offset by their higher rate of postterm births requiring obstetric intervention (17.6% vs. 13.7%).

Adverse effects, including rates of hemorrhage and antenatal hospitalization, did not differ between the two study groups. The only adverse event that occurred more often in the DHA group than in the controls was:

The Australian National Health and Medical Research Council funded the DOMINO study. Dr. Makrides reported serving on scientific advisory boards for Nestle, Fonterra, and Nutricia.

Neither the mean cognitive scores nor the mean language scores differed significantly between children of mothers who took fish oil supplements and children of the control mothers. Similarly, scores on measures of motor coordination and social-emotional behavior, and adaptive behavior were not significantly different.

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A Noteworthy Finding

One noteworthy finding of the DOMINO trial is that women who took fish oil supplements had a significantly lower risk of very preterm birth (defined as delivery before 34 weeks’ gestation) than did women in the control group, said Dr. Emily Oken and Dr. Mandy B. Belfort.

The rate of very preterm birth was 1.1% with DHA-rich supplements (13 such births), compared with 2.3% with placebo (27 such births). The downstream benefits of that difference included lower rates of early and late birth weight, fewer admissions to the neonatal intensive care unit, and a nonsignificant 30% reduction in infant mortality.

Although the absolute numbers of these outcomes were small, the relative benefits were large, they noted.

“For now, pregnant women should take care to get the recommended intake of 200 mg/day of DHA, either by including low-mukeyric, high-DHA fish, or by consuming a daily n-3 PUFA (polyunsaturated fatty acid) supplement. The benefit of higher intakes remains unclear,” Dr. Oken and Dr. Belfort concluded.

Dr. Oken is at Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston. Dr. Belfort is at Children’s Hospital Boston. Neither Dr. Oken nor Dr. Belfort reported any financial disclosures. The comments were taken from their editorial accompanying the report (JAMA 2010;304:1717-8).