Effect of a fish-oil concentrate on serum lipids in postmenopausal women

This question-and-answer commentary is by Bruce Holub and Ken Stark, Department of Human Biology and Nutritional Sciences, University of Guelph, Guelph, Ontario, Canada N1G 2W1. The first part consists of a synopsis of a paper written by Stark and Holub with E.J. Park and V.A. Maines (Effect of a Fish-Oil Concentrate on Serum Lipids in Postmenopausal Women Receiving and Not Receiving Hormone Replacement Therapy in a Placebo-Controlled, Double-Blind Trial., Am. J. Clin. Nutr. 72:89–94, 2000), followed by the commentary.

Synopsis of the original study

Background. Dietary supplementation with omega-3 (n-3) fatty acids has been shown to lower serum triglyceride (TG) concentrations in studies of mainly male subjects. The effects of omega-3 fatty acid supplementation on postmenopausal women taking and not taking hormone replacement therapy (HRT) have not been fully investigated.

Objective. To elucidate the effect of a fish oil-derived omega-3 fatty acid concentrate on serum lipid/lipoprotein risk factors for cardiovascular disease (CVD) in postmenopausal women taking or not taking HRT, particularly serum TG concentrations and the TG/high-density lipoprotein-cholesterol (HDL-C) ratio.

Design. Thirty-six postmenopausal women were recruited for a randomized placebo-controlled trial. Subjects were grouped according to exogenous hormone use and then randomized to either eight placebo oil capsules per day (control) or eight omega-3 enriched capsules per day (treatment). The treatment group received 2.4 g of eicosapentaenoic acid (EPA) plus 1.6 g of docosahexaenoic acid (DHA) per day. On day 0 and day 28 of the experiment, samples were collected for determination of serum lipids and the fatty acid composition of serum phospholipids.

Results. The omega-3 supplementation significantly lowered serum TG concentrations by 26% (P < 0.0001), and the overall ratio of serum TG/HDL-C was significantly reduced by 28% (P < 0.01) in postmenopausal women. Treatment markedly enhanced the concentrations of EPA and DHA in serum phospholipid (P < 0.05).

Conclusions. These results show that supplementation with a fish oil-derived concentrate can favorably influence selected CVD risk factors, particularly a marked lowering of serum TG and the TG/HDL-C ratio in postmenopausal women taking or not taking HRT. These results have the potential to reduce the risk of coronary heart disease by 27% for postmenopausal women.

Commentary

Q: Please tell us about the rationale for your study.

A: Coronary heart disease (CHD) risk in women increases dramatically with the onset of menopause. For this reason, we have been particularly interested in nutritional means to reduce CHD risk in postmenopausal women—both those receiving and not receiving HRT. Furthermore, a number of risk factors associated with CHD in this group of women are undermanaged. A moderate elevation in fasting TG levels (10 mg/100 mL) increases the risk for cardiovascular disease in both men and women, with the magnitude of the risk being significantly greater in the latter (5.7 vs. 13.6%) based on a recent meta-analysis. Unfortunately, clinical management of TG levels in most women is often not considered unless the fasting TG level is above 200 mg/100 mL even though the literature indicates that a
moderate rise in TG (above 100 mg/100 mL) increases risk for CHD. We have estimated that 50 to 75% of North American postmenopausal women fall within the latter “risk category” with respect to their circulating TG status. In addition, recent evidence indicates that the ratio of fasting TG/HDL-C is a strong predictor of myocardial infarction risk.

This risk indicator (TG/HDL-C) was another target of our nutritional supplementations using omega-3 fatty acids in the form of a fish-oil concentrate. After grouping postmenopausal women according to exogenous hormone use, they were randomly allocated to receive 4 g/d of omega-3 fatty acids in the form of EPA/DHA combined or an omega-6 fatty acid placebo (evening primrose oil). Results indicated that supplementation with the fish-oil-derived concentrate could, within 28 d of intervention, significantly lower serum TG concentrations and the TG/HDL-C ratio. The use of omega-3 fatty acid supplementation (as EPA/DHA) was estimated to reduce the risk of CHD by approximately 27% in our postmenopausal women.

Furthermore, the enrichment of serum phospholipid (the biomarker for EPA plus DHA) was of interest based on epidemiological and other studies showing cardioprotective potential for omega-3 fatty acids when those levels are increased in the circulation concomitant with higher intakes.

Q: Why did you use an encapsulated fish-oil concentrate containing both EPA and DHA?
A: Insufficient data are available in the literature to establish either EPA or DHA alone as being superior to the
other for cardioprotection. A mixture of the two fatty acids may be preferable. We anticipated from previous research trials that an approximate 7 to 8% reduction in serum TG levels might be expected per gram of omega-3 fatty acid consumed (EPA plus DHA combined). Since patented pharmaceutical agents used for TG lowering, which are a major cost to the Canadian public health care system, provide TG-lowering in the 25 to 30% range, we anticipated that 4 g/d of omega-3 fatty acid supplementation could possibly generate "drug-like" reductions in TG levels at a fraction of the cost of the aforementioned pharmaceutical agents in a nutraceutical form.

Q: **How do you extrapolate 26% lower serum TG level after fish-oil supplementation to a predicted reduction in heart disease risk of approximately 27% in postmenopausal women?**

A: Based on published studies showing the relationship between relative risk of CHD in women and their corresponding TG blood concentration, it was calculated that the observed lowering in serum TG levels could be extrapolated to a predicted 27% reduction in heart disease risk in postmenopausal women. Furthermore, a 24% reduction in the combined outcome of death from coronary heart disease, nonfatal myocardial infarction, and stroke, resulted from an approximate 30% reduction in TG over five years with the drug gemfibrozil in men with heart disease.

Q: **Were there any side effects to fish oils such as low-density lipoprotein**

**into food without losing its soul.**
(LDL)-cholesterol elevation, or belching and flatulence?

A: No significant alterations in LDL-cholesterol were observed, and belching was rather infrequent and did not pose any apparent difficulty in our subjects maintaining compliance throughout the study. Following conclusion of the supplementation, the blinding of the subjects with respect to their intervention was considered to be successful since only 56% of the subjects in the fish-oil group guessed their treatment correctly whereas random guessing would result in 50% of the subjects being able to identify their treatment correctly. Subject compliance with the study protocol was determined to be consistently high, based on gas-liquid chromatographic analyses of the fatty acid composition of serum phospholipid (a useful biomarker for compliance to the supplementation).

Q: You mentioned you examined both women receiving and not receiving HRT. Did you find any differences between groups?

A: We found no statistically significant differences in serum lipids between women receiving and not receiving HRT, although the overall mean TG-lowering was 19% in the former and 35% in the latter. These differences may be clinically significant and may warrant further investigation in larger trials. Although many observational studies indicated that HRT decreases CVD risk, results from recent intervention trials have failed to confirm CVD risk reduction as predicted by earlier studies. To complicate the issue, there are many different types of HRT available. In general, oral delivery of HRT is often associated with changes in the serum lipid profile including increased TG while transdermal delivery results in no or minor changes in serum lipids. All the subjects in our study were receiving HRT orally, and the TG-lowering found in this group would be expected to offset TG increases associated with oral estrogen use as demonstrated by past studies.

Bibliography


