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Randomized, crossover, head-to-head comparison of EPA and DHA supplementation to reduce inflammation markers in men and women: the Comparing EPA to DHA Study[1–3]

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ABSTRACT

Background: To date, most studies on the anti-inflammatory effects of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in humans have used a mixture of the 2 fatty acids in various forms and proportions.

Objectives: We compared the effects of EPA supplementation with those of DHA supplementation (re-esterified triacylglycerol; 90% pure) on inflammation markers (primary outcome) and blood lipids (secondary outcome) in men and women at risk of cardiovascular disease.

Design: In a double-blind, randomized, crossover, controlled study, healthy men (n = 48) and women (n = 106) with abdominal obesity and low-grade systemic inflammation consumed 3 g/d of the following supplements for periods of 10 wk: *1*) EPA (2.7 g/d), *2*) DHA (2.7 g/d), and *3*) corn oil as a control with each supplementation separated by a 9-wk washout period. Primary analyses assessed the difference in cardiometabolic outcomes between EPA and DHA.

Results: Supplementation with DHA compared with supplementation with EPA led to a greater reduction in interleukin-18 (IL-18) ($-7.0\% \pm 2.8\%$ compared with $-0.5\% \pm 3.0\%$, respectively; P = 0.01) and a greater increase in adiponectin ($3.1\% \pm 1.6\%$ compared with $-1.2\% \pm 1.7\%$, respectively; $P < 0.001$). Between DHA and EPA, changes in CRP ($-7.9\% \pm 5.0\%$ compared with $-1.8\% \pm 6.5\%$, respectively; P = 0.25), IL-6 ($-12.0\% \pm 7.0\%$ compared with $-13.4\% \pm 7.0\%$, respectively; P = 0.86), and tumor necrosis factor-α ($-14.8\% \pm 5.1\%$ compared with $-7.6\% \pm 10.2\%$, respectively; P = 0.63) were NS. DHA compared with EPA led to more pronounced reductions in triglycerides ($-13.3\% \pm 2.3\%$ compared with $-11.9\% \pm 2.2\%$, respectively; P = 0.005) and the cholesterol:HDL-cholesterol ratio ($-2.5\% \pm 1.3\%$ compared with $0.3\% \pm 1.1\%$, respectively; P = 0.006) and greater increases in HDL cholesterol ($7.6\% \pm 1.4\%$ compared with $-0.7\% \pm 1.1\%$, respectively; $P < 0.0001$) and LDL cholesterol ($6.9\% \pm 1.8\%$ compared with $2.2\% \pm 1.6\%$, respectively; P = 0.04). The increase in LDL-cholesterol concentrations for DHA compared with EPA was significant in men but not in women (P-treatment $\times$ sex interaction = 0.046).

Conclusions: DHA is more effective than EPA in modulating specific markers of inflammation as well as blood lipids. Additional studies are needed to determine the effect of a long-term DHA supplementation per se on cardiovascular disease risk. This trial was registered at clinicaltrials.gov as NCT01810003. *Am J Clin Nutr* doi: 10.3945/ajcn.116.131896.

Keywords: DHA, EPA, inflammation, men and women, randomized controlled trial, risk factors

INTRODUCTION

Subclinical inflammation is recognized as a key etiologic factor in the development of atherosclerosis that leads to ischemic heart disease (IHD).[8] (1, 2). There is a growing body of literature that has suggested that long-chain ω-3 (n–3) PUFAs (LCn–3PUFAs), primarily EPA (20:5n–3) and DHA (22:6n–3), may attenuate the proinflammatory state that is associated with obesity and metabolic syndrome (MetS) (3). In that regard, a number of mechanisms supporting the purported anti-inflammatory effects of LCn–3PUFAs have been proposed. These mechanisms include the inhibition of the proinflammatory nuclear transcription factor κB in various

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[2] The Canadian Institutes for Health Research was not involved in designing the study; conducting the study; the collection, management, analysis, or interpretation of the data; or preparation and review of the manuscript before submission.

[3] Supplemental Tables 1–6 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

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[8] Abbreviations used: apoB, apolipoprotein B; CRP, C-reactive protein; CVD, cardiovascular disease; IHD, ischemic heart disease; ITT, intent to treat; LCn–3PUFA, long chain ω-3 (n–3) PUFA; MetS, metabolic syndrome; RCT, randomized controlled trial.

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