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Fish oil supplementation alters circulating eicosanoid concentrations in young healthy men

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ARTICLE INFO

Article history:
Received 13 December 2012
Accepted 13 February 2013

Keywords:
Prostaglandin-F2α
Thromboxane-B2
Triglyceride
Inflammation
Omega-3

ABSTRACT

Objective. Increasing omega-3 fatty acid (FA) intake, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), is associated with numerous health benefits; however, the benefits on inflammation appear to vary depending on the study population examined. While improvements in inflammatory status have been reported in the elderly, there is less evidence regarding the effects of fish oil supplementation on inflammation in young adults. The goal of the present study was to examine the influence of fish oil supplementation on lipid metabolites and the inflammatory status of young healthy men.

Materials/Methods. Fasted serum samples were collected from 10 young healthy males (23.4 ± 1.7 years) before and after a 3-month supplementation of fish-oil containing 2.0 g EPA and 1.0 g DHA. Samples were analyzed to investigate changes in FA profiles, bioclinical parameters (e.g. triglyceride and hs-CRP), and a panel of 26 eicosanoids. Paired t-tests were used to evaluate changes between the time points.

Results. Serum triglycerides decreased ($P = 0.0006$) while the proportion of HDL-c (relative to total cholesterol) increased significantly ($P = 0.0495$) after fish oil supplementation. Specific monounsaturated and polyunsaturated FA levels were changed following supplementation, including reductions in palmitoleic and oleic acid, and, as expected, increases in EPA and DHA. We also observed increases in eicosanoids, namely prostaglandin-F2α ($P < 0.0001$) and thromboxane-B2 ($P = 0.0296$), after fish oil supplementation.

Conclusions. A 3-month fish oil supplementation in young healthy men improved circulating triglyceride levels and the HDL-c ratio while, concomitantly, increasing the concentrations of two eicosanoids (prostaglandin-F2α and thromboxane-B2). This suggests that fish oil supplementation does have significant benefits in young healthy adults and that specific omega-6-derived eicosanoids can help to further our understanding regarding the beneficial link between omega-3 FA and inflammation.

Abbreviations: BMI, Body Mass Index; MUFA, Monounsaturated fatty acid; PUFA, Polyunsaturated fatty acid; EPA, Eicosapentaenoic Acid; DHA, Docosahexaenoic Acid; HDL-c, High-density lipoprotein cholesterol; LDL-c, Low-density lipoprotein cholesterol; TXB2, Thromboxane-B2; PGF2α, Prostaglandin-F2α; HETE, hydroxyeicosatetraenoic acid; COX, Cyclooxygenase; LOX, Lipoxygenase.

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0026-0495/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.metabol.2013.02.004

1. Introduction

First noted in Greenland Inuit, the consumption of cold-water marine animals was thought to contribute towards the favourable blood lipid profile in residents of arctic communities (e.g. low blood cholesterol and triglyceride levels) [1]. Subsequent research has generated evidence regarding the beneficial metabolic outcomes associated with the consumption of fish oils enriched with long-chain omega-3 polyunsaturated fatty acids (PUFAs) — namely, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) [2,3]. Previous work has demonstrated that these fatty acids (FAs) are positively associated with anti-inflammatory proteins (e.g. adiponectin) and inversely associated with markers of inflammation (e.g. interleukin-6 and tumor necrosis factor-α) [4,5].

Due to the strong associations between omega-3 FA and inflammation, there is now considerable interest to elucidate the various molecular mechanisms by which EPA and DHA can influence inflammatory pathways. One mechanism that has attracted recent interest concerns the ability of EPA and DHA to regulate the production of pro-inflammatory eicosanoids (such as 2-series thromboxanes and prostaglandins) [2,6]. Eicosanoids and docosanoids are a class of lipid metabolites that are generated from 20- and 22-carbon fatty acids (FAs), respectively; with recognized pro- or anti-inflammatory properties that are dependent on the FA from which they were derived (i.e. n6 or n3). Pro-inflammatory eicosanoids are produced primarily from arachidonic acid (AA, n6) via the cyclooxygenase (COX-1 or -2) and lipoxygenase (LOX-5,-12 or -15) pathways [7,8]. These AA-derived eicosanoids have been positively associated with pathological conditions such as cardiovascular disease and type-2 diabetes [9,10]. Anti-inflammatory eicosanoids and docosanoids are produced primarily from EPA and DHA metabolism via the COX and LOX pathways. In contrast to AA-derived eicosanoids, EPA- and DHA-derived eicosanoids are related to favourable health benefits, such as improving insulin-sensitivity and reducing inflammation [11–13].

Dietary supplementation of EPA and DHA has been previously shown to improve a range of metabolic parameters (e.g. insulin sensitivity, inflammation, and blood lipids) in several population subgroups, including premenopausal women with a pre-existing inflammatory phenotype and elderly adults [14,15]. These studies and others provide evidence for the benefits of fish oil consumption in elderly and diseased populations towards improved health; however, less work has been presented concerning the effects of fish oil consumption in healthy individuals who show little to no evidence of inflammation or disease. Therefore, the purpose of the present study was to better understand the potential health benefits of fish oil supplementation in young healthy males, with a specific focus on circulating lipid metabolites and inflammatory profiles.

2. Methods

2.1. Patient recruitment

Twelve physically active males (18–30 years of age) free from cardiovascular complications and currently enrolled at the University of Guelph were recruited through a campus-wide poster campaign. Individuals were screened by telephone questionnaire and excluded if they exhibited any one of the following criteria: (i) daily consumption of herbal supplements; (ii) medicated; (iii) history of respiratory or heart problems (at rest or exercise); (iv) hypercholesterolemia; (v) hypertension; (vi) diabetes mellitus; (vii) smoking; (viii) prone to bleeding, bruising, or fainting; (ix) scheduled hospitalization or surgery in the next 3-months; (x) physical inactivity or exercise more than 4×/week; and/or (xi) allergies to local freezing, fish, or fish oil capsules. Individuals that reported routine consumption of n3-rich foods (e.g. salmon, flax-seeds, and n3-fortified items) were also excluded. The study was approved by the Human Research Ethics Board of the University of Guelph and all participants provided written consent.

2.2. Omega-3 supplementation

Pre-packaged doses of Omega-3 Complete capsules (Jamieson Laboratories Ltd., Windsor, ON, Canada) were provided to each participant prior to study commencement. Each capsule contained 400 mg of EPA and 200 mg of DHA (refined from fish oils). Participants were asked to consume 5 capsules per day in order to obtain a daily dose of 2.0 g of EPA and 1.0 g of DHA. The dose of fish oil and the supplementation period used in the present study are similar to those used in a number of previous studies [16–18].

2.3. Analysis of blood parameters

Following an overnight fast, serum samples were collected at the Human Nutraceutical Research Unit (University of Guelph, Guelph, ON, Canada) from participants at two time points: baseline (T0) and after the 3-month fish oil supplementation (T3). Serum samples were used to measure triglyceride, total cholesterol, LDL-c, HDL-c, and high-sensitivity C-reactive protein (hs-CRP). The analysis of the aforementioned parameters was conducted by Life Labs Medical Laboratory Services (Kitchener, ON, Canada). The remaining serum samples were aliquoted and stored at −80 °C for FA and eicosanoid analyses.

2.4. Fatty acid analysis

Serum samples from T0 and T3 were analyzed to assess relative changes in FA composition for each participant. All solvents and reagents were obtained from Fisher Scientific (Toronto, ON, Canada). Isolation, extraction, and quantification of total FA were performed as previously described [19]. Briefly, lipids were extracted from serum samples and saponified for 1 h at 100 °C in a 0.5 M KOH in methanol solution, followed by methylation with hexane and 14% BF3-MeOH at 100 °C for 1.5 h. Samples were then analyzed using an Agilent Technologies 7890A GC system (Agilent Technologies, Mississauga, ON, CA). Peaks were identified by comparison to FA methyl ester standards suspended in hexane. Individual FA values were calculated as a percentage of total peak area. All data are reported as % FA ± SE. FAs contributing to <0.25% of the total FA profile were excluded from analysis.