Clinical Research Summaries using DHA advantage (i.e. "life's dha")

Algal-oil capsules and cooked salmon: nutritionally equivalent sources of docosahexaenoic acid.

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Food and nutrition professionals question whether supplement-sourced nutrients appear to be equivalent to those derived from natural food sources. We compared the nutritional availability of docosahexaenoic acid (DHA) from algal-oil capsules to that from assayed cooked salmon in 32 healthy men and women, ages 20 to 65 years, in a randomized, open-label, parallel-group study. In this 2-week study comparing 600 mg DHA/day from algal-oil capsules to that from assayed portions of cooked salmon, mean change from baseline in plasma phospholipids and erythrocyte DHA levels was analyzed and DHA levels were compared by Student's t tests. In post-hoc analyses to determine bioequivalence, least-squares mean ratios of percent change from baseline in plasma phospholipid and erythrocyte DHA levels were compared. DHA levels increased by approximately 80% in plasma phospholipids and by approximately 25% in erythrocytes in both groups. Changes in DHA levels in plasma phospholipids and erythrocytes were similar between groups. As measured by delivery of DHA to both plasma and erythrocytes, fish and algal-oil capsules were equivalent. Both regimens were generally well-tolerated. These results indicate that algal-oil DHA capsules and cooked salmon appear to be bioequivalent in providing DHA to plasma and red blood cells and, accordingly, that algal-oil DHA capsules represent a safe and convenient source of non-fish-derived DHA.
PMID: 18589030 [PubMed - indexed for MEDLINE]

Bioequivalence of Docosahexaenoic acid from different algal oils in capsules and in a DHA-fortified food.

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Docosahexaenoic acid (DHA), a long-chain omega-3 fatty acid, is important for eye and brain development and ongoing visual, cognitive, and cardiovascular health. Unlike fish-sourced oils, the bioavailability of DHA from vegetarian-sourced (algal) oils has not been formally assessed. We assessed bioequivalence of DHA oils in capsules from two different algal strains versus bioavailability from an algal-DHA-fortified food. Our 28-day randomized, placebo-controlled, parallel group study compared bioavailability of (a) two different algal DHA oils in capsules ("DHASCO-T"
and "DHASCO-S") at doses of 200, 600, and 1,000 mg DHA per day (n = 12 per group) and of (b) an algal-DHA-fortified food (n = 12). Bioequivalence was based on changes in plasma phospholipid and erythrocyte DHA levels. Effects on arachidonic acid (ARA), docosapentaenoic acid-n-6 (DPAn-6), and eicosapentaenoic acid (EPA) were also determined. Both DHASCO-T and DHASCO-S capsules produced equivalent DHA levels in plasma phospholipids and erythrocytes. DHA response was dose-dependent and linear over the dose range, plasma phospholipid DHA increased by 1.17, 2.28 and 3.03 g per 100 g fatty acid at 200, 600, and 1,000 mg dose, respectively. Snack bars fortified with DHASCO-S oil also delivered equivalent amounts of DHA on a DHA dose basis. Adverse event monitoring revealed an excellent safety and tolerability profile. Two different algal oil capsule supplements and an algal oil-fortified food represent bioequivalent and safe sources of DHA.

PMID: 17713804 [PubMed - indexed for MEDLINE]

**Validation of a rapid measure of blood PUFA levels in humans.**

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An assay involving a finger stick and filter paper blood spotting was developed to determine polyunsaturated fatty acid (PUFA) levels in blood. Capillary whole blood from a finger stick was blotted on antioxidant impregnated filter paper, air dried, saponified and methylated using sodium hydroxide and boron trifluoride in methanol. The method differed from those described previously because separation of plasma and red blood cells (RBCs) was not needed, thin-layer chromatography (TLC) was not required to separate phospholipids, initial extraction of lipids before transesterification was not necessary, and the fatty acid methyl ester (FAME) method was able to methylate steryl esters, free fatty acids, and sphingomyelins. Twenty-six subjects provided blood samples by finger stick and venipuncture. Levels of long-chain polyunsaturated fatty acids (LC-PUFA) from capillary whole blood were correlated with those from RBCs and PLs in venous blood (P < 0.001, R(2) ranged from 0.64 to 0.86). Although highly significant (P < 0.002), the R(2) values for the correlation between arachidonic acid (ARA) levels in capillary whole blood with ARA levels in RBCs and plasma phospholipids (PLs) were relatively lower (R(2) = 0.31-0.41, respectively). Results indicate that the described finger stick assay represents a fast, reliable method to measure specific LC-PUFA levels.

PMID: 18084784 [PubMed - indexed for MEDLINE]

**Effects of docosahexaenoic acid on serum lipoproteins in patients with combined hyperlipidemia: a randomized, double-blind, placebo-controlled trial.**

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OBJECTIVE: The objective of this study was to evaluate the effects of daily dietary supplementation with 1.25 g or 2.5 g of docosahexaenoic (DHA), in the absence of eicosapentaenoic acid (EPA), on serum lipids and lipoproteins in persons with combined hyperlipidemia (CHL) [serum low-density lipoprotein cholesterol (LDL-C) 130 to 220 mg/dL and triglycerides 150 to 400 mg/dL]. METHODS: After a 6-week dietary stabilization period, subjects entered a 4-week single-blind placebo (vegetable oil) run-in phase. Those with adequate compliance during the run-in were randomized into one of three parallel groups (placebo, 1.25, or 2.5 g/day DHA) for 6 weeks of treatment. Supplements were administered in a triglyceride form contained in gelatin capsules. Primary outcome measurements were plasma phospholipid DHA content, serum triglycerides, high-density lipoprotein cholesterol (HDL-C), LDL-C and non-HDL-C.

RESULTS: The DHA content of plasma phospholipids increased dramatically (2 to 3 fold) in a dose-dependent manner. Significant (p < 0.05) changes were observed in serum triglycerides (17 to 21% reduction) and HDL-C (6% increase) which were of similar magnitude in both DHA groups. Non-HDL-C [+1.6 (NS) and +5.7% (p < 0.04)] and LDL-C [+9.3% (NS) and +13.6% (p < 0.001)] increased in the DHA treatment groups. All lipid effects reached an apparent steady state within the first 3 weeks of treatment.

CONCLUSION: Dietary DHA, in the absence of EPA, can affect lipoprotein cholesterol and triglyceride levels in patients with combined hyperlipidemia. The desirable triglyceride and HDL-C changes were present at a dose which did not significantly increased non-HDL-C or LDL-C. These preliminary findings suggest that dietary supplementation with 1.25 g DHA/day, provided in a triglyceride form, may be an effective tool to aid in the management of hypertriglyceridemia.

PMID: 9176830 [PubMed - indexed for MEDLINE]


Docosahexaenoic acid restores endothelial function in children with hyperlipidemia: results from the EARLY study.

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OBJECTIVE: The primary objective of this study was to determine whether the National Cholesterol Education Program Step II (NCEP-II) diet or supplementation with docosahexaenoic acid (DHA) with the diet, affects endothelial function in children with familial hypercholesterolemia (FH) or the phenotype of familial combined hyperlipidemia (FCH). As secondary endpoints, the influence of diet and DHA supplementation on lipid profiles as well as biomarkers for oxidative stress and inflammation, and asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthase, were all evaluated. METHODS: In a double-blind, placebo-controlled, randomized, crossover study design, 20 children (ages 9-19 years) with FH (n = 12) and FCH (n = 8) received nutritional counseling based on the National
Cholesterol Education Program Step II (NCEP-II) and food guide pyramid dietary guidelines for 6 weeks. They were then randomly assigned to supplementation with docosahexaenoic acid (DHA 1.2 g/d) or placebo for 6 weeks, followed by a washout phase of 6 weeks and crossover phase of 6 weeks while continuing the NCEP-II diet. Endothelium-dependent flow-mediated dilation (FMD) of the brachial artery was determined by high-resolution ultrasound. Plasma levels of total cholesterol, triglycerides and lipoprotein classes (LDL, HDL, VLDL) were measured by ultracentrifugation and enzymatic methods, plasma F2 isoprostanes by gas chromatography/mass spectrometry, urinary 8-OH-2' deoxyguanosine by liquid chromatography, high sensitivity C-reactive protein by immunonephelometry and ADMA by liquid chromatography.

RESULTS: FMD increased significantly after DHA supplementation compared to baseline (p < 0.001), diet alone (p < 0.002), placebo (p < 0.012) and washout (p < 0.001) phases of the study without affecting biomarkers for oxidative stress, inflammation or ADMA. DHA supplementation was associated with increased levels of total cholesterol (p < 0.01), LDL- and HDL cholesterol concentrations (p < 0.001) compared to the NCEP-II diet.

CONCLUSION: This study demonstrates that DHA supplementation restores endothelial-dependent FMD in hyperlipidemic children. The endothelium may thus be a therapeutic target for DHA. This is consistent with a hypothesis of increasing NO bioavailability, with the potential for preventing the progression of early coronary heart disease in high-risk children.

PMID: 15624283 [PubMed - indexed for MEDLINE]

Effect of docosahexaenoic acid on lipoprotein subclasses in hyperlipidemic children (the EARLY study).


To test the hypothesis that a dietary omega-3 fatty acid, docosahexaenoic acid, improves the lipoprotein subclass profile of children who have hyperlipidemia, we conducted a randomized, double-blind, placebo-controlled study. Children who had hyperlipidemia (n = 20) were stabilized on a low-fat diet for 6 weeks and then randomized to receive 1.2 g/day of docosahexaenoic acid for 6 weeks or placebo. Supplementation with docosahexaenoic acid significantly increased low-density lipoprotein subclass 1 and high-density lipoprotein subclass 2 (large and buoyant; less atherogenic particles) by 91% and 14%, respectively, compared with the placebo phase. Low-density lipoprotein subclass 3 (small and dense; more atherogenic particles) decreased by 48%.

PMID: 15781019 [PubMed - indexed for MEDLINE]
Docosahexaenoic acid supplementation decreases remnant-like particle-cholesterol and increases the (n-3) index in hypertriglyceridemic men.

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Plasma remnant-like particle-cholesterol (RLP-C) and the RBC (n-3) index are novel risk factors for cardiovascular disease. Effects of docosahexaenoic acid (DHA) supplementation on these risk factors in hypertriglyceridemic men have not been studied. We determined effects of DHA supplementation on concentrations of plasma RLP-C, the RBC (n-3) index, and associations between concentrations of plasma RLP-C with those of plasma lipids and fatty acids. Hypertriglyceridemic men aged 39-66 y, participated in a randomized, placebo-controlled, parallel study. They received no supplements for 8 d and then received either 7.5 g/d DHA oil (3 g DHA/d) or olive oil (placebo) for the last 90 d. Fasting blood samples were collected on study d -7, 0 (baseline), 45 (mid-intervention), 84, and 91 (end-intervention). DHA supplementation for 45 d decreased (P < 0.05) fasting RLP-C (36%) and increased plasma eicosapentaenoic acid (EPA):arachidonic acid (AA) (100%) and the RBC (n-3) index (109%). Continued supplementation with DHA between d 45 and 91 further increased the RBC (n-3) index (162%) and plasma EPA:AA (137%) compared with baseline values. RLP-C concentration was positively associated (P < 0.01) with the plasma concentrations of triacylglycerols (Kendall's correlation coefficient or r = 0.46), triacylglycerol:HDL cholesterol (HDL-C) (r = 0.44), total cholesterol:HDL-C (r = 0.26), Apo B (r = 0.22), C III (r = 0.41), and E (r = 0.17), and 18:1(n-9) (r = 0.32); it was negatively associated (P < 0.05) with plasma concentrations of DHA (r = -0.32), EPA (r = -0.25), HDL-C (r = -0.21), LDL cholesterol:Apo B (r = -0.30), and HDL-C:Apo A (r = -0.25). Supplementation with placebo oil did not alter any of the response variables tested. Decreased atherogenic RLP-C and increased cardio-protective (n-3) index may improve cardiovascular health.

PMID: 18156400 [PubMed - indexed for MEDLINE]
double-blind, randomized, placebo-controlled parallel study. They received no supplements for the first 8 d and received either 7.5 g DHA oil/d (3 g DHA/d) or olive oil (placebo) for the last 90 d. Lipoprotein particle diameters and concentrations were measured by nuclear magnetic resonance spectroscopy.

RESULTS: DHA supplementation for 45 d significantly (P < 0.05) decreased concentrations of fasting triacylglycerol (24%), large VLDL (92%), and intermediate-density lipoproteins (53%) and the mean diameter of VLDL particles (11.1 nm). It elevated concentrations of LDL cholesterol (12.6%), small VLDL particles (133%), and large LDL particles (120%) and the mean diameter of LDL particles (0.6 nm) in fasting plasma. Similar changes were observed for area under the curve for postprandial samples (0-6 h); however, the number of small dense LDL particles decreased significantly (21%), and the change in LDL cholesterol was not significant. Continued supplementation with DHA beyond 45 d caused no further changes; placebo treatment altered none of the responses tested.

CONCLUSION: DHA supplementation may improve cardiovascular health by lowering concentrations of triacylglycerols and small, dense LDL particles.

PMID: 17684201 [PubMed - indexed for MEDLINE]

Docosahexaenoic Acid (DHA) But Not Eicosapentaenoic Acid (EPA) Prevents Trans-10, Cis-12 Conjugated Linoleic Acid (CLA)-Induced Insulin Resistance in Mice.

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Background: The objective of this study was to investigate if eicosapentaenoic acid (20:5n-3, EPA) or docosahexaenoic acid (22:6n-3, DHA) or both would prevent conjugated linoleic acid (CLA)-induced insulin resistance and fatty liver. Methods: Eight-week-old, pathogen-free C57BL/6N female mice (10 per group) were fed either a control diet or diets containing t10, c12-CLA (0.5 wt %), CLA + DHA (0.5% + 1.5 wt %), or CLA + EPA (0.5% + 1.5 wt %) for 8 weeks prior to sacrifice and tissue collection. Results: CLA supplementation caused an 8.9-fold increase in circulating insulin, a 2.6-fold increase in liver weight, and a 6.2-fold increase in the weight of total lipids in the liver as compared with the corresponding values in the control group. DHA prevented the CLA-induced insulin resistance, while EPA was ineffective. Both EPA and DHA prevented CLA-induced fatty liver and reduced weights of total liver lipids to the levels of the control group. CLA also reduced the plasma leptin and adiponectin concentrations to approximately 15% of those in the control group. Both EPA and DHA partially restored the CLA-induced decrease in leptin, but only DHA partially restored the plasma adiponectin.

Conclusions: Our results suggest that DHA but not EPA in fish oils may reduce insulin resistance which may be mediated through an increase in circulating adiponectin. These findings may have clinical implications in the dietary management of patients at risk of insulin resistance and diabetes.

PMID: 18370801 [PubMed - in process]
Lipid responses to a dietary docosahexaenoic acid supplement in men and women with below average levels of high density lipoprotein cholesterol.

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OBJECTIVE: To assess fasting lipid responses to a docosahexaenoic acid (DHA) supplement in men and women with below-average levels of high-density lipoprotein (HDL) cholesterol.

METHODS: This randomized, double-blind, controlled clinical trial included 57 subjects, 21-80 years of age, with fasting HDL cholesterol concentrations \(<\) or \(\leq\)44 mg/dL (men) and \(<\) or \(\leq\)54 mg/dL (women), but \(>\) or \(\geq\)35 mg/dL. Subjects were randomly assigned to receive either 1.52 g/day DHA from capsules containing DHA-rich algal triglycerides or olive oil (control) for six weeks.

RESULTS: There were no significant differences between groups in baseline lipid values. The DHA supplemented group showed significant changes \([-43\ (DHA)\ vs.\ -14\ (controls)\ mg/dL,\ p = 0.015]\) and percent changes \([-21\%\ (DHA)\ vs.\ -7\%\ (controls),\ p = 0.009]\) in triglycerides, total (12 vs. 3 mg/dL; p = 0.021 and 6% vs. 2%; p = 0.018) and low-density lipoprotein (17 vs. 3 mg/dL; p = 0.001 and 12% vs. 3%; p = 0.001) cholesterol concentrations, and in the triglyceride to HDL cholesterol ratio (-1.33 vs. -0.50, p = 0.010), compared with controls. In addition, there was a significant reduction in the percentage of LDL cholesterol carried by small, dense particles in the DHA supplemented group (changes = -10% vs. -3%, p = 0.025).

CONCLUSIONS: Supplementation with 1.52 g/d of DHA in men and women with below-average HDL cholesterol concentrations raised the LDL cholesterol level, but had favorable effects on triglycerides, the triglyceride/HDL cholesterol ratio and the fraction of LDL cholesterol carried by small, dense particles. Further research is warranted to evaluate the net impact of these alterations on cardiovascular risk.

PMID: 15930485 [PubMed - indexed for MEDLINE]
factors was evaluated using a double-blind randomised placebo-controlled parallel-design trial in thirty-nine men and forty women. Subjects received 4 g oil/d for 4 weeks; the active treatment provided 1.5 g DHA and 0.6 g DPA. Active treatment increased plasma concentrations of arachidonic acid, adrenic acid, DPA and DHA by 21, 11, 11 and 88 mg/l respectively and the proportions of DPA and DHA in erythrocyte phospholipids by 78 and 27 % respectively. Serum total, LDL- and HDL-cholesterol increased by 0.33 mmol/l (7.3 %), 0.26 mmol/l (10.4 %) and 0.14 mmol/l (9.0 %) compared with placebo (all P < or =0.001). Factor VII (FVII) coagulant activity increased by 12 % following active treatment (P = 0.006). There were no significant differences between treatments in LDL size, blood pressure, plasma glucose, serum C-reactive protein, plasma FVII antigen, FVII activated, fibrinogen, von Willebrand factor, tocopherol or carotenoid concentrations, plasminogen activator inhibitor-1, creatine kinase or troponin-I activities, haematology or liver function tests or self-reported adverse effects. Overall, the oil was well tolerated and did not adversely affect cardiovascular risk.

PMID: 16512939 [PubMed - indexed for MEDLINE]

The triglyceride-lowering effects of a modest dose of docosahexaenoic acid alone versus in combination with low dose eicosapentaenoic acid in patients with coronary artery disease and elevated triglycerides.

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BACKGROUND: Hypertriglyceridemia is a risk factor for coronary artery disease (CAD). The American Heart Association recommends 1000 mg of omega-3 fatty acids, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), daily for cardioprotection and higher doses for triglyceride-lowering in patients with CAD.

METHODS: This was a prospective, randomized, double-blind study comparing DHA to DHA + EPA in patients with CAD and triglycerides greater than 200 mg/dL. Subjects were randomized to either 1000 mg of DHA or 1252 mg of DHA + EPA for eight weeks. Baseline and eight-week laboratories were drawn to assess changes in the fasting lipid profile. The primary objective was to evaluate the change in triglycerides between the two groups at eight weeks.

RESULTS: A total of 116 subjects were enrolled; 57 in the DHA group and 59 in the DHA + EPA group. Baseline characteristics were similar between groups. The mean age was 69.4 +/- 9.1 years and 70.7% were male. Triglycerides decreased by an average of 21.8% in the DHA group (p < 0.001) and 18.3% in the DHA + EPA group (p < 0.001). The difference between groups was not significant. A greater proportion of subjects in the DHA group achieved triglyceride goal (less than 150 mg/dL) compared to the DHA + EPA group (24.6% versus 10.2%, p < 0.05).

CONCLUSIONS: Our results indicate that the American Heart Association recommended cardioprotective dose of omega-3 fatty acids can also significantly
lower triglycerides in patients with CAD. There do not appear to be significant
differences in triglyceride-lowering between DHA only and DHA + EPA combination
products when dosing is based on DHA.
PMID: 17229894 [PubMed - indexed for MEDLINE]

Differential eicosapentaenoic acid elevations and altered cardiovascular
disease risk factor responses after supplementation with docosahexaenoic
acid in postmenopausal women receiving and not receiving hormone
replacement therapy.

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BACKGROUND: Dietary docosahexaenoic acid (DHA) has triacylglycerol-lowering
potential and undergoes in vivo retroconversion to eicosapentaenoic acid (EPA) in
humans. Hormone replacement therapy (HRT) influences circulating lipid
concentrations and fatty acid metabolism. DHA supplementation has not been
studied in postmenopausal women. OBJECTIVE: We studied the effects of
supplementation with DHA (free of EPA) on the resulting elevation in EPA and on
selected cardiovascular disease risk factors in postmenopausal women. DESIGN:
Women receiving (n = 18) and not receiving (n = 14) HRT completed a
randomized, double-blind, placebo-controlled crossover trial with a DHA supplement
(2.8 g DHA/d). A washout period of > or =6 wk divided the two 28-d intervention
periods. Fasting blood samples were collected for analysis. RESULTS: In all women,
DHA supplementation was associated with significant changes (P < 0.05), including
20% lower serum triacylglycerol concentrations, 8% higher HDL-cholesterol
concentrations, a 28% lower overall ratio of serum triacylglycerol to HDL
cholesterol, and a 7% decrease in resting heart rate. DHA supplementation resulted
in a 45% lower net increase (P = 0.02) in EPA and a 42% lower (P = 0.0028)
estimated percentage retroconversion of DHA to EPA [DeltaEPA/(DeltaEPA +
DeltaDHA) x 100] in women receiving than in those not receiving HRT.
CONCLUSION: With DHA supplementation, the accumulation of EPA in serum
phospholipids is significantly attenuated in postmenopausal women receiving HRT
compared with that in women not receiving HRT. DHA supplementation can also
favorably influence selected cardiovascular disease risk factors in postmenopausal
women.
PMID: 15113713 [PubMed - indexed for MEDLINE]

LDL cholesterol-raising effect of low-dose docosahexaenoic acid in middle-
aged men and women.

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BACKGROUND: Long-chain n-3 polyunsaturated fatty acids have variable effects on LDL cholesterol, and the effects of docosahexaenoic acid (DHA) are uncertain.

OBJECTIVE: The objective of the study was to determine the effect on blood lipids of a daily intake of 0.7 g DHA as triacylglycerol in middle-aged men and women.

DESIGN: Men and women aged 40-65 y (n = 38) underwent a double-blind, randomized, placebo-controlled, crossover trial of treatment with 0.7 g DHA/d for 3 mo.

RESULTS: DHA supplementation increased the DHA concentration in plasma by 76% (P < 0.0001) and the proportion in erythrocyte lipids by 58% (P < 0.0001). Values for serum total cholesterol, LDL cholesterol, and plasma apolipoprotein B concentrations were 4.2% (0.22 mmol/L; P = 0.04), 7.1% (0.23 mmol/L; P = 0.004), and 3.4% (P = 0.03) higher, respectively, with DHA treatment than with placebo. In addition, the LDL cholesterol:apolipoprotein B ratio was 3.1% higher with DHA treatment than with placebo (P = 0.04), which suggested an increase in LDL size. Plasma lathosterol and plant sterol concentrations were unaffected by treatment.

CONCLUSION: A daily intake of approximately 0.7 g DHA increases LDL cholesterol by 7% in middle-aged men and women. It is suggested that DHA down-regulates the expression of the LDL receptor.

PMID: 15051597 [PubMed - indexed for MEDLINE]
rate tended to be 2.1 beats/min lower after DHA treatment than after the placebo period (P = 0.15). The results indicate that a moderate increase in the daily intake of DHA to approximately 0.7 g DHA lowers diastolic BP but does not influence indices of endothelial function or arterial stiffness in the short term.

PMID: 17374663 [PubMed - indexed for MEDLINE]

Incorporation of n-3 fatty acids into plasma lipid fractions, and erythrocyte membranes and platelets during dietary supplementation with fish, fish oil, and docosahexaenoic acid-rich oil among healthy young men.

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The effects of n-3 fatty acid supplementation in the form of fresh fish, fish oil, and docosahexaenoic acid (DHA) oil on the fatty acid composition of plasma lipid fractions, and platelets and erythrocyte membranes of young healthy male students were examined. Altogether 59 subjects (aged 19-32 yr, body mass index 16.8-31.3 kg/m2) were randomized into the following diet groups: (i) control group; (ii) fish diet group eating fish meals five times per week [0.38 +/- 0.04 g elcosapentaenoic acid (EPA) and 0.67 +/- 0.09 g DHA per day]; (iii) DHA oil group taking algae-derived DHA oil capsules (1.68 g/d DHA in triglyceride form); and (iv) fish oil group (1.33 g EPA and 0.95 g DHA/d as free fatty acids) for 14 wk. The fatty acid composition of plasma lipids, platelets, and erythrocyte membranes was analyzed by gas chromatography. The subjects kept 4-d food records four times during the study to estimate the intake of nutrients. In the fish diet, in DHA oil, and in fish oil groups, the amounts of n-3 fatty acids increased and those of n-6 fatty acids decreased significantly in plasma lipid fractions and in platelets and erythrocyte membranes. A positive relationship was shown between the total n-3 polyunsaturated fatty acids (PUFA) and EPA and DHA intake and the increase in total n-3 PUFA and EPA and DHA in all lipid fractions analyzed. DHA was preferentially incorporated into phospholipid (PL) and triglyceride (TG) and there was very little uptake in cholesterol ester (CE), while EPA was preferentially incorporated into PL and CE. The proportion of EPA in plasma lipids and platelets and erythrocyte membranes increased also by DHA supplementation, and the proportion of linoleic acid increased in platelets and erythrocyte membranes in the DHA oil group as well. These results suggest retroconversion of DHA to EPA and that DHA also interferes with linoleic acid metabolism.

PMID: 9252957 [PubMed - indexed for MEDLINE]
Effect of maternal docosahexaenoic acid supplementation on postpartum depression and information processing.

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OBJECTIVE: The purpose of this study was to determine the effect of docosahexaenoic acid supplementation on plasma phospholipid docosahexaenoic acid content and indices of depression and information processing for women who breast-feed. STUDY DESIGN: Mothers who planned to breast-feed their infants were assigned randomly in a double-masked fashion to receive either docosahexaenoic acid (approximately 200 mg/d) or placebo for the first 4 months after the delivery. Major outcome variables included plasma phospholipid fatty acid patterns and scores on a self-rating questionnaire of current depression symptoms. A structured clinical interview of depression, scores on another self-rating questionnaire of depression symptoms, and a laboratory measure of information processing were obtained in subgroups of the total population.

RESULTS: Plasma phospholipid contents of docosahexaenoic acid at baseline were 3.15 +/- 0.78 and 3.31 +/- 0.70 (mg/dL of total fatty acids) in the docosahexaenoic acid and placebo groups, respectively. After 4 months, the plasma phospholipid docosahexaenoic acid content of the docosahexaenoic acid group was 8% higher (3.40 +/- 0.97 mg/dL), whereas that of the placebo group was 31% lower (2.27 +/- 0.87 mg/dL). Despite the higher plasma phospholipid docosahexaenoic acid content of the supplemented group after 4 months, there was no difference between groups in either self-rating or diagnostic measures of depression; information processing scores of the two groups also did not differ.

CONCLUSION: Docosahexaenoic acid supplementation (approximately 200 mg/d) for 4 months after the delivery prevented the usual decline in plasma phospholipid docosahexaenoic acid content of women who breastfeed but did not influence self-ratings of depression, diagnostic measures of depression, or information processing. PMID: 12748510 [PubMed - indexed for MEDLINE]


Effects of docosahexaenoic acid supplementation on blood lipids, estrogen metabolism, and in vivo oxidative stress in postmenopausal vegetarian women.

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BACKGROUND: Vegetarians are generally deficient in long-chain n-3 fatty acids. Long-chain n-3 fatty acids have a beneficial effect on plasma lipid levels, and some studies showed that they had breast cancer suppression effect. One of the biomarkers of breast cancer risk is the ratio of urinary 2-hydroxyestrone (2-
OHE(1)) to 16alpha-hydroxyestrone (16alpha-OHE(1)). OBJECTIVE: To investigate the effect of docosahexaenoic acid (DHA, 22:6n-3) supplementation on blood lipids, estrogen metabolism and oxidative stress in vegetarians. DESIGN: Single-blind, randomized, placebo-controlled trial. INTERVENTIONS: Twenty-seven postmenopausal vegetarian women were recruited. After a 2-week run-in period with 6 g placebo corn oil, the subjects were subsequently randomized to receive either 6 g corn oil (n=13) or 6 g DHA-rich algae oil (2.14 g of DHA/day) (n=14) for 6 weeks. Two subjects in corn oil group withdrew before completion. MAIN OUTCOME MEASURES: Plasma lipids, urinary 2-OHE(1) and 16alpha-OHE(1), urinary F(2)-isoprostanes and plasma alpha-tocopherol.

RESULTS: Plasma LDL-DHA and EPA level increased significantly by DHA supplementation. DHA decreased plasma cholesterol (C) levels (P=0.04), but did not influence the levels of plasma TG, LDL-C and HDL-C, alpha-tocopherol, urinary F(2)-isoprostanes, 2-OHE(1), 16alpha-OHE(1) and ratio of 2-OHE(1) to 16alpha-OHE(1) as compared to corn oil.

CONCLUSION: DHA supplementation at a dose of 2.14 g/day for 42 days decreases plasma cholesterol but neither does it show beneficial effects on estrogen metabolism, nor does it induce deleterious effects on the observed in vivo antioxidant or oxidative stress marker in postmenopausal vegetarian women.

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PMID: 16278686 [PubMed - indexed for MEDLINE]

Fish diet, fish oil and docosahexaenoic acid rich oil lower fasting and postprandial plasma lipid levels.

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OBJECTIVE: The present study was carried out to clarify the effects of fish diet, fish oil and docosahexaenoic acid (DHA) rich oil on fasting and postprandial lipid levels in healthy male students. DESIGN: The study was a randomized single-blind study with a control and three study groups. SETTING: The study was carried out in the Departments of Physiology and Clinical Nutrition of University of Kuopio. SUBJECTS: Healthy male volunteers were recruited for the study from the university student population. Fifty-nine subjects entered and 55 completed the study.

INTERVENTIONS: For 15 weeks the subjects in the fish diet group ate 4.3 +/- 0.5 fish containing meals per week and those in the fish oil and DHA-oil groups ate 4 g oil per day. Fish diet provided 0.38 +/- 0.04 g eicosapentaenoic acid (EPA) and 0.67 +/- 0.09 g DHA, fish oil 1.33 g EPA and 0.95 g DHA and DHA-oil (EPA-free) 1.68 g DHA per day.

RESULTS: Fasting plasma triglyceride levels decreased in all test groups in 14 weeks when compared to the control group (P < 0.05). Total plasma cholesterol
levels did not change but the HDL2/HDL3-cholesterol ratio increased in all test
groups by over 50% (P < 0.05). The postprandial total and chylomicron triglyceride
responses, measured as areas under the response curve, were lowered in 15 weeks
by the fish diet and fish oil (P < 0.05), the same tendency (P < 0.1) being seen in
DHA-oil group.

CONCLUSIONS: These results show that both fasting and postprandial triglyceride
concentrations can be decreased with moderate intakes of long-chain n-3 fatty
acids either from a fish diet or fish oil and that also pure DHA has a
hypotriglyceridemic effect.
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Fatty acid composition of erythrocyte, platelet, and serum lipids in strict
vegans.

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The fatty acid composition of erythrocytes, platelets, and serum lipids was
compared between subjects who had been eating a strict uncooked vegan diet
("living food") for years and omnivore controls. The vegan diet contains equal
amounts of fat but more monounsaturated and polyunsaturated and less saturated
fatty acids than the mixed diet of the control group. In vegans, the proportion of
linoleic acid was greater in all lipid fractions studied. Also, the levels of other n-6
fatty acids were greater, with the exception of arachidonic acid levels, which were
similar in most fractions. In erythrocytes, platelets and serum phospholipid
fractions, this increase was mainly at the expense of the n-3 fatty acids. The
proportions of eicosapentaenoic and docosahexaenoic acid were only 29-36% and
49-52% of those in controls, respectively. In vegans the ratio of n-3 to n-6 fatty
acids was only about half that in omnivores. In addition to the lower levels of n-3
fatty acids, the proportions of palmitic and stearic acids were lower in serum
cholesterol esters, triglycerides and free fatty acids of vegans. The proportion of
oleic acid was slightly lower only in serum cholesteryl esters and erythrocyte
phosphatidylserine. The results show that, in the long term, the vegan diet has little
effect on the proportions of oleic and arachidonic acids, whereas the levels of n-3
fatty acids are depressed to very low levels with prolonged consumption of the high
linoleic and oleic acid components of this diet.
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Hemostatic factors and platelet aggregation after a fish-enriched diet or
fish oil or docosahexaenoic acid supplementation.
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The effects of a fish-enriched diet or dietary supplements consisting of either fish oil or a docosahexaenoic acid-rich oil (DHA-oil) on platelet aggregation and hemostatic factors were studied in healthy male students. After an experimental period of 15 weeks, the levels of tissue factor pathway inhibitor, prothrombin fragment 1+2 and fibrinogen as well as factor VII activity were not changed. Factor X activity was slightly decreased by the fish diet (P < 0.05). Collagen but not ADP-induced maximum platelet aggregation decreased in the fish diet and the fish oil groups (P < 0.05 in both). In the DHA-oil group there was a slight, statistically insignificant, increase of platelet aggregation which correlated significantly with the decrease of plasma triglycerides. Platelet aggregation measured 4 h after a standardized fat meal was lower than in the fasting state and this decrease correlated with the increase of plasma triglycerides. These results show that a fish diet and fish oil, but not DHA-oil, inhibit in vitro platelet aggregation and that hemostatic factors are not affected by moderate n-3 fatty acid supplementation.
PMID: 9430389 [PubMed - indexed for MEDLINE]
RESULTS: FMD increased significantly after DHA supplementation compared to baseline (p < 0.001), diet alone (p < 0.002), placebo (p < 0.012) and washout (p < 0.001) phases of the study without affecting biomarkers for oxidative stress, inflammation or ADMA. DHA supplementation was associated with increased levels of total cholesterol (p < 0.01), LDL- and HDL cholesterol concentrations (p < 0.001) compared to the NCEP-II diet.

CONCLUSION: This study demonstrates that DHA supplementation restores endothelial-dependent FMD in hyperlipidemic children. The endothelium may thus be a therapeutic target for DHA. This is consistent with a hypothesis of increasing NO bioavailability, with the potential for preventing the progression of early coronary heart disease in high-risk children.

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Supplementation with an algae source of docosahexaenoic acid increases (n-3) fatty acid status and alters selected risk factors for heart disease in vegetarian subjects.

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The purpose of this double-blind study was to investigate the influence of dietary supplementation with an algae source of docosahexaenoic acid [DHA; 22:6(n-3)], devoid of any eicosapentaenoic acid [EPA; 20:5(n-3)], on serum/platelet DHA status, the estimated retroconversion of DHA to EPA, and risk factors for heart disease in vegetarian subjects. Healthy vegetarians (12 male, 12 female) consumed nine capsules daily of either DHA (1.62 g/d) or corn oil for 6 wk. Consumption of DHA capsules increased DHA levels in serum phospholipid by 246% (from 2.4 to 8.3 g/100 g fatty acids) and in platelet phospholipid by 225% (from 1.2 to 3.9 g/100 g fatty acids). EPA levels increased in serum phospholipid by 117% (from 0.57 to 1.3 g/100 g fatty acids) and in platelet phospholipid by 176% (0.21 to 0.58 g/100 g fatty acids) via metabolic retroconversion; the estimated extent of DHA retroconversion to EPA was 11.3 and 12.0%, based on the serum and platelet analyses, respectively. Arachidonic acid [AA; 20:4(n-6)] levels in serum and platelet phospholipids decreased moderately during the trial period (DHA group) as did both docosapentaenoic acids [22:5(n-6) and 22:5(n-3)].

Although no significant changes were found in the total and LDL-cholesterol levels with DHA supplementation, the total cholesterol:HDL-cholesterol ratio showed a moderate decrease over time as did the LDL-cholesterol:HDL-cholesterol ratio and serum triglyceride concentrations. DHA supplementation did not alter the various thrombogenic factors measured. In conclusion, DHA supplementation markedly enhanced the DHA status (of serum and platelets), provided for the formation of substantial EPA, and lowered the total and LDL-cholesterol:HDL-cholesterol ratios.

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Docosahexaenoic Acid (DHA) But Not Eicosapentaenoic Acid (EPA) Prevents Trans-10, Cis-12 Conjugated Linoleic Acid (CLA)-Induced Insulin Resistance in Mice.

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Background: The objective of this study was to investigate if eicosapentaenoic acid (20:5n-3, EPA) or docosahexaenoic acid (22:6n-3, DHA) or both would prevent conjugated linoleic acid (CLA)-induced insulin resistance and fatty liver. Methods: Eight-week-old, pathogen-free C57BL/6N female mice (10 per group) were fed either a control diet or diets containing t10, c12-CLA (0.5 wt %), CLA + DHA (0.5% + 1.5 wt %), or CLA + EPA (0.5% + 1.5 wt %) for 8 weeks prior to sacrifice and tissue collection. Results: CLA supplementation caused an 8.9-fold increase in circulating insulin, a 2.6-fold increase in liver weight, and a 6.2-fold increase in the weight of total lipids in the liver as compared with the corresponding values in the control group. DHA prevented the CLA-induced insulin resistance, while EPA was ineffective. Both EPA and DHA prevented CLA-induced fatty liver and reduced weights of total liver lipids to the levels of the control group. CLA also reduced the plasma leptin and adiponectin concentrations to approximately 15% of those in the control group. Both EPA and DHA partially restored the CLA-induced decrease in leptin, but only DHA partially restored the plasma adiponectin. Conclusions: Our results suggest that DHA but not EPA in fish oils may reduce insulin resistance which may be mediated through an increase in circulating adiponectin. These findings may have clinical implications in the dietary management of patients at risk of insulin resistance and diabetes.

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