Asthma bronchiale

Nagakura T, Matsuda S, Shichijyo K, Sugimoto H, Hata K.  
Dietary supplementation with fish oil rich in omega-3 polyunsaturated fatty acids in children with bronchial asthma.  
Omega-3 polyunsaturated fatty acids have anti-inflammatory effects in vitro, and high dietary levels are associated with a lower incidence of inflammatory diseases. However, only limited effects have been demonstrated in asthma. The effects of dietary supplementation with fish oil for 10 months in 29 children with bronchial asthma was investigated in a randomized controlled fashion. In order to minimize the effects of environmental inhaled allergens and diet, this study was performed in a long-term treatment hospital. Subjects received fish oil capsules containing 84 mg eicosapentaenoic acid (EPA) and 36 mg docosahexaenoic acid (DHA) or control capsules containing 300 mg olive oil. The daily dosages of EPA and DHA were 17.0-26.8 and 7.3-11.5 mg x kg body weight(-1), respectively. Asthma symptom scores decreased and responsiveness to acetylcholine decreased in the fish oil group but not in the control group. In addition, plasma EPA levels increased significantly only in the fish oil group (p<0.0088). No significant side-effects were observed. The present results suggest that dietary supplementation with fish oil rich in the omega-3 polyunsaturated fatty acids eicosapentaenoic acid and docosahexaenoic acid is beneficial for children with bronchial asthma in a strictly controlled environment in terms of inhalant allergens and diet.

Spector SL, Surette ME.  
Diet and asthma: has the role of dietary lipids been overlooked in the management of asthma?  
Ann Allergy Asthma Immunol 2003 Apr;90(4):371-7; quiz 377-8, 421  
OBJECTIVE: This article discusses the role of diet in the management of asthma. Readers will gain an understanding of how evolution of the western diet has contributed to increased asthma prevalence and how dietary modification that includes management of dietary lipids may reduce symptoms of asthma. DATA SOURCES: Relevant studies published in English were reviewed. STUDY SELECTION: Medline search to identify peer-reviewed abstracts and journal articles. RESULTS: Asthma and obesity, which often occur together, have increased in prevalence in recent years. Studies suggest adaption of a western diet has not only contributed to obesity, but that increased intake of specific nutrients can cause changes in the frequency and severity of asthma. Increased asthma prevalence has also been proposed to arise from increased exposure to diesel particles or lack of exposure to infectious agents or endotoxins during childhood, generating a biased Th2 immune response, and increased cytokine and leukotriene production. Antagonists directed against these pro-inflammatory mediators include anticytokines and antileukotrienes. A reduction in the levels of inflammatory mediators associated with asthma has also been seen with dietary interventions, such as the administration of oils containing gamma-linolenic acid and eicosapentaenoic acid. CONCLUSIONS: Evidence suggests elevated body mass index and dietary patterns, especially intake of dietary lipids, contribute to symptoms of asthma. Dietary modification may help patients manage their asthma as well as contribute to their overall health.
Dietary supplementation with very long-chain n-3 fatty acids in man decreases expression of the interleukin-2 receptor (CD25) on mitogen-stimulated lymphocytes from patients with inflammatory skin diseases. Eur J Clin Invest 1994 Apr;24(4):236-42

T-cell activation and cytokine production play an important role in several chronic inflammatory diseases. Because n-3 fatty acids exert beneficial effects on the clinical state of some of these diseases, we examined the effect of dietary supplementation of n-3 fatty acids on T-cell proliferation, expression of CD25 (interleukin-2 receptor alpha-chain), secretion of interleukin-2, interleukin-6 and tumour necrosis factor from T-cells from patients with psoriasis and atopic dermatitis. During 4 months, 21 patients supplied 6 g of highly concentrated ethyl esters of EPA and DHA in gelatin capsules daily to their diet. In the control group 20 patients supplied 6 g per day of corn oil in gelatin capsules to their diet. Eicosapentaenoic acid (20:5, n-3) of serum phospholipids increased from 14 (min 4-max 42) to 81 (min 59-max 144) mg l-1 (P < 0.01) in patients with atopic dermatitis receiving n-3 fatty acids, and from 25 (min 7-max 66) to 74 (min 46-max 142) mg l-1 (P < 0.01) in patients with psoriasis, whereas docosahexaenoic acid (22:6, n-3) increased from 65 (min 46-max 120) to 92 (min 54-max 121) mg l-1 (P < 0.05) and from 81 (min 38-max 122) to 92 (min 63-max 169) mg l-1 (NS) in atopic and psoriatic patients, respectively. The changes in the serum phospholipid fatty acid profile in the groups receiving n-3 fatty acids, correlate to the dietary intake of corresponding fatty acids.(ABSTRACT TRUNCATED AT 250 WORDS)
Colitis ulzerosa


OBJECTIVE: To determine the efficacy of fish oil supplementation in patients with active ulcerative colitis. DESIGN: Multicenter, randomized, double-blind, placebo-controlled, crossover trial with 4-month treatment periods (fish oil and placebo) separated by a 1-month washout. SETTING: Four gastroenterology divisions. PATIENTS: Twenty-four patients with active ulcerative colitis entered the study. Five dropped out, and one was noncompliant. Eighteen patients completed the study. All patients had active disease as manifested by diarrhea and rectal inflammation. INTERVENTIONS: Treatment with prednisone and sulfasalazine was continued. Fish oil supplementation consisted of 18 Max-EPA (eicosapentaenoic acid) capsules daily (eicosapentaenoic acid, 3.24 g; and docosahexaenoic acid, 2.16 g). Placebo supplementation consisted of 18 identical capsules containing isocaloric amounts of vegetable oil. MEASUREMENTS: Patients were evaluated at study entry and after each diet period. Evaluations included a review of symptoms, flexible sigmoidoscopy, rectal biopsy, and rectal dialysis to measure prostaglandin E2 and leukotriene B4 levels. RESULTS: Fish oil supplementation resulted in a significant decrease in rectal dialysate levels of leukotriene B4 from 71.0 to 27.7 pg/mL (average change, -43.3 pg/mL; 95% CI, -83 to -3.6). Significant improvements were seen in acute histology index (average change, -8.5 units from a baseline of 10.5 units; CI, -12.9 to -4.2) and total histology index (average change, -8.5 units from a baseline of 14.80; CI, -13.2 to -3.8) as well as significant weight gain (average weight gain, 1.74 kg, CI, 0.94 to 2.54). No significant changes occurred in any variable during the placebo period. Seven patients received concurrent treatment with prednisone. During the fish oil supplementation period, the mean prednisone dose decreased from 12.9 mg/d to 6.1 mg/d and rose from 10.4 mg/d to 12.9 mg/d during the placebo diet period (P greater than 0.20). CONCLUSIONS: Four months of diet supplementation with fish oil in patients with inflammatory bowel disease resulted in reductions in rectal dialysate leukotriene B4 levels, improvements in histologic findings, and weight gain.
Depressionen


Patients with depression have been extensively reported to be associated with the abnormality of omega-3 polyunsaturated fatty acids (PUFAs), including significantly low eicosapentaenoic acid and docosahexaenoic acid in cell tissue contents (red blood cell membrane, plasma, etc.) and dietary intake. However, more evidence is needed to support its relation. In this study, we conducted an 8-week, double-blind, placebo-controlled trial, comparing omega-3 PUFAs (6.6 g/day) [corrected] with placebo, on the top of the usual treatment, in 28 patients with major depressive disorder. Patients in the omega-3 PUFA group had a significantly decreased score on the 21-item Hamilton Rating Scale for Depression than those in the placebo group (P < 0.001). From the preliminary findings in this study, omega-3 PUFAs could improve the short-term course of illness and were well tolerated in patients with major depressive disorder.


OBJECTIVE: Studies have reported that countries with high rates of fish oil consumption have low rates of depressive disorder. The authors studied a specific omega-3 fatty acid, the ethyl ester of eicosapentaenoic acid (E-EPA), as an adjunct to treatment for depressive episodes occurring in patients with recurrent unipolar depressive disorder who were receiving maintenance antidepressant therapy. METHOD: Twenty patients with a current diagnosis of major depressive disorder participated in a 4-week, parallel-group, double-blind addition of either placebo or E-EPA to ongoing antidepressant therapy. Seventeen of the patients were women, and three were men. RESULTS: Highly significant benefits of the addition of the omega-3 fatty acid compared with placebo were found by week 3 of treatment. CONCLUSIONS: It is not possible to distinguish whether E-EPA augments antidepressant action in the manner of lithium or has independent antidepressant properties of its own.

Locke CA, Stoll AL. Omega-3 fatty acids in major depression. World Rev Nutr Diet 2001;89:173-85

Geographic areas where consumption of DHA is high are associated with decreased rates of depression. DHA deficiency states, such as alcoholism and the postpartum period, also are linked with depression. Individuals with major depression have marked depletions in omega-3 FAs (especially DHA) in erythrocyte phospholipids compared with controls. These data suggest that DHA may be associated with depression, and the limited data available on supplementation with DHA or other omega-3 FAs seem to support the hypothesis that DHA may have psychotropic effects. Overall, the use of EFAs is promising, particularly in view of the many illnesses potentially treatable with these substances; however, larger, carefully designed studies are needed to establish whether DHA is an effective and safe antidepressant, mood stabilizer, or antipsychotic. A few preliminary trials of DHA are in progress, but no studies comparing DHA against placebo or against an established antidepressant have been carried out. Studies to address this issue are being developed at the Massachusetts General Hospital. Studies likely will require escalating doses of DHA, eventually reaching high levels so as to ensure that patients will avoid a potentially ineffective subclinical dose. Careful monitoring of dietary intake among subjects also will necessary because a high intake of omega-3-rich foods may confound results. Finally, large-scale, placebo-controlled, double-blind trials comparing the efficacy and safety of DHA against standard antidepressants are required before psychiatrists can recommend DHA therapy as effective and safe for the treatment of depression and other mood disorders. Given the popularity of self-medication by patients who already are taking marketed antidepressants, studies examining the use of DHA as an augmentor to standard antidepressants may answer whether DHA can occupy a niche as an augmenting agent for patients who have made a partial response or have not responded to conventional antidepressants. Considering that natural medications generally seem best for treating mild to moderate illness, the role of DHA as a therapy for minor and subsyndromal depression also should be considered. It is hoped that studies of these types will help to clarify some of the knowledge gaps outlined in this article.
Hyperlipoproteinämie

n-3 fatty acids and serum lipoproteins: human studies.
Am J Clin Nutr 1997 May;65(5 Suppl):1645S-1654S

The effects of n-3 fatty acids from fish oils (eicosapentaenoic acid and docosahexaenoic acid) and plant oils (alpha-linolenic acid) on human serum lipids and lipoproteins are reviewed. Studies were included in this review if they were placebo-controlled, crossover, or parallel design studies providing < 7 g n-3 fatty acids/d and with treatment periods of > or = 2 wk duration. Only three studies were available for evaluation of the effects of alpha-linolenic acid on serum lipid concentrations. From these studies it appeared that alpha-linolenic acid (18:3n-3) was equivalent to n-6-rich oils vis-vis lipid and lipoprotein effects. Only when very large amounts of flaxseed oil were fed did the hallmark effect of marine n-3 fatty acids-reduced triacylglycerol concentrations-appear. Thus, in terms of effects on lipoprotein metabolism, the plant-derived n-3 fatty acid is not equivalent to the marine-based acids.

More studies using the marine-based acids were examined and summarized. Both crossover (n = 36) and parallel (n = 29) design studies reached the same conclusions: total cholesterol is not materially affected by n-3 fatty acid consumption, low-density-lipoprotein cholesterol concentrations tend to rise by 5-10% and high-density-lipoprotein cholesterol by 1-3%, and serum triacylglycerol concentrations decrease by 25-30%. These effects of marine n-3 fatty acids are now well-established; what remains is to determine the mechanisms behind these effects and, more importantly, their health consequences.

Nonpharmacologic treatment of hypertriglyceridemia: focus on fish oils.
Clin Cardiol 1999 Jun;22(6 Suppl):II40-3

Early studies in Greenland Eskimos stimulated interest in evaluating the effect of Omega-3 fatty acids on coronary artery disease. Subsequent studies showed a significant decrease in triglyceride levels in patients receiving high doses of fish oil containing DHA and EPA. Slight increases in LDL were also observed in patients receiving fish oil supplements. These studies have also shown a dose-response effect which persists as long as supplementation continues. Later trials, specifically the Diet and Reinfarction Trial and the Indian Experiment of Infarct Survival, have demonstrated a reduction in cardiac death rates and in the incidence of cardiac symptoms in patients receiving fish oil.

Triglyceride-lowering effect of omega-3 LC-polyunsaturated fatty acids--a review.

There is increasing evidence that serum triglycerides are a significant and independent risk factor for CVD. The aim of this report is to review recent literature pertinent to the triglyceride-lowering effect of omega-3 long chain polyunsaturated fatty acids (LC-PUFA). Animal data are not considered because they are difficult to extrapolate to the human situation. A large body of evidence derived from epidemiological studies and clinical trials has consistently demonstrated that this effect is dose-dependent and can be achieved by diet. The smallest amount of omega-3 LC-PUFA needed to significantly lower serum triglycerides appears to be approximately 1 g/day as provided by a fish diet. Use of fish oil administering as little as 0.21 g EPA and 0.12 g DHA per day significantly lowered serum triglycerides in hyperlipidemics. In normolipidemics, a daily intake of 0.17 g EPA and 0.11 g DHA, given as a fish oil supplement, induced a non-significant reduction of 22%. These findings must be considered as preliminary and warrant further research. Intake of omega-3 LC-PUFA is frequently reported to modestly increase LDL cholesterol. However, in normo- or slightly hyperlipidemic individuals who received omega-3 LC-PUFA for 4 months or longer, changes of LDL cholesterol were not significantly different from a placebo group. Both EPA and DHA lower serum triglycerides, but they may have a differential effect on lipoproteins. Intake of omega-3 LC-PUFA in the amount mentioned above is safe.

Effect of fish oil on LDL oxidation and plasma homocysteine concentrations in health.
J Lab Clin Med 2003 Jan;141(1):41-9

Oxidation of low-density lipoprotein (LDL) and hyperhomocysteinemia are believed to play a role in therogenesis. Whether n-3 polyunsaturated fatty acids increase LDL susceptibility to oxidation or influence homocysteine (Hcy) metabolism has long been a subject of controversy. In this study, we evaluated the effect of 8 weeks of dietary supplementation with 6 g/day of fish oil (FO; 3 g of n-3 fatty acids) on plasma lipoproteins, in vitro LDL peroxidation, antioxidant status, and plasma Hcy
concentrations in 16 normolipidemic subjects. FO rapidly and significantly (P < .01) decreased plasma total and very low density lipoprotein triglyceride concentrations and had no effect on LDL or high-density-lipoprotein cholesterol. The mean lag time before onset of Cu(2+)-induced LDL oxidation, as well as plasma and LDL alpha-tocopherol and beta-carotene concentrations, was unchanged. However, changes in plasma aminothiol concentrations occurred during the study. Specifically, a progressive and significant increase in total Hcy plasma concentrations was observed (13.4% and 20% after 4 and 8 weeks, respectively; P < .01). Total glutathione concentrations were significantly higher after 8 weeks (P < .05). The tHcy increase was not associated with changes in plasma folate or vitamin B(12) concentrations. However, concentrations of plasma nitric oxide metabolites (NO(x) = NO(2) + NO(3)) were significantly higher than at baseline after 8 weeks of FO intake (74%; P < .01). Further, the changes in total Hcy and NO(x) plasma concentrations observed after 8 weeks of FO were found to be significantly correlated (r = .78, P < .001). With this study, we report for the first time the apparent interaction of n-3 fatty acids and nitric oxide on Hcy metabolism.


Eight normolipidaemic volunteers, habitual partial skim milk drinkers and non-eaters of fish during the study, were given 500 ml day(-1) of partial skim milk for 1 month; they were then switched to 500 ml day(-1) of a novel commercially available milk preparation, supplying 400 mg of N-3 fatty acids-of which 300 mg were EPA+DHA-and 15 mg vitamin E, for 6 weeks. No changes in plasma lipid parameters were observed after the first run-in month; at 3 and 6 weeks on the N-3-rich milk, marked increments of plasma EPA (44 and 31%, respectively) and DHA (13 and 31%, respectively) were observed. Triacylglycerol (TG) concentrations decreased by 19% and high-density lipoprotein (HDL) concentrations increased by 19% at 6 weeks; plasma vitamin E rose by 21% while the susceptibility of plasma to oxidation was unaffected. Correlations were found between plasma EPA or DHA and TG, cholesterol, and HDL. In conclusion, the intake of a milk preparation providing low amounts of EPA+DHA to healthy individuals led to marked increases of N-3 fatty acids and vitamin E in plasma and in associated favourable changes in HDL and TG.


BACKGROUND: The influence of the quality of dietary fat on some aspects of lipid metabolism-i.e. lipoprotein concentrations, post-prandial lipids and LDL size-is not completely understood, especially in healthy individuals. OBJECTIVES: Aim of this study was to evaluate the effects of different types of dietary fat (monounsaturated vs. saturated fatty acids, and n-3 or placebo supplementation) on fasting lipoproteins, LDL size and post-prandial lipids in healthy people. DESIGN: One hundred and sixty-two individuals were randomly assigned to follow two isoenergetic diets, one rich in saturated fatty acids (SFA diet) and the other in monounsaturated fatty acids (MUFA diet). Each group was further randomised to receive supplementation with fish oil (3.6 g/day) or placebo. RESULTS: The type of diet significantly affected LDL cholesterol and triacylglycerol content, which was higher with the SFA diet and lower with the MUFA diet. The changes between the two diets were statistically significant for cholesterol (P<0.01) and triacylglycerol (P<0.03). VLDL cholesterol and triacylglycerol were significantly reduced and LDL cholesterol significantly increased by fish oil supplementation. Plasma triacylglycerol was significantly lower in those taking n-3 fatty acids, also 1 and 3 h after a test-meal. Neither type of diet nor n-3 supplementation affected LDL size. CONCLUSIONS: A moderate substitution of saturated fatty acids with monounsaturated fatty acids has beneficial effects on lipid metabolism also in healthy individuals. A moderate supplementation of long-chain n-3 fatty acids in healthy individuals reduces both fasting and post-prandial triacylglycerol concentrations but increases LDL cholesterol, irrespective of the type of diet.


The n-3 fatty acids of fish and fish oil have great potential for the prevention and treatment of patients with coronary artery disease. Unlike many of the pharmaceutical agents used in patients with coronary artery disease that have just a single mechanism of action, the eicosapentaenoic and docosahexaenoic acids of fish oil have multifaceted actions. One of their most important effects is the
prevention of arrhythmias, with documentation derived from experiments in cultured myocytes, experiments in animals, epidemiologic correlations, and clinical trials. Especially important is the ability of these n-3 fatty acids to inhibit ventricular fibrillation and consequent cardiac arrest. Eicosapentaenoic acid has several antithrombotic actions, particularly in inhibiting the synthesis of thromboxane A2, the prostaglandin that causes platelet aggregation and vasoconstriction. Fish oil retards the growth of the atherosclerotic plaque by inhibiting both cellular growth factors and the migration of monocytes. The n-3 fatty acids promote the synthesis of the beneficial nitric oxide in the endothelium. Experiments in humans indicate a profound hypolipidemic effect of fish oil, especially lowering of plasma triacylglycerol. Both very-low-density lipoprotein production and apolipoprotein B synthesis are inhibited by fish oil. Finally, fish oil has a mild blood pressure-lowering effect in both normal and mildly hypertensive individuals. These composite effects suggest a prominent therapeutic role for fish oil in the prevention and treatment of coronary artery disease.
Connor SL, Connor WE.
Are fish oils beneficial in the prevention and treatment of coronary artery disease?
The n-3 fatty acids of fish and fish oil have great potential for the prevention and treatment of patients with coronary artery disease. Unlike many of the pharmaceutical agents used in patients with coronary artery disease that have just a single mechanism of action, the eicosapentaenoic and docosahexaenoic acids of fish oil have multifaceted actions. One of their most important effects is the prevention of arrhythmias, with documentation derived from experiments in cultured myocytes, experiments in animals, epidemiologic correlations, and clinical trials. Especially important is the ability of these n-3 fatty acids to inhibit ventricular fibrillation and consequent cardiac arrest. Eicosapentaenoic acid has several antithrombotic actions, particularly in inhibiting the synthesis of thromboxane A2, the prostaglandin that causes platelet aggregation and vasoconstriction. Fish oil retards the growth of the atherosclerotic plaque by inhibiting both cellular growth factors and the migration of monocytes. The n-3 fatty acids promote the synthesis of the beneficial nitric oxide in the endothelium. Experiments in humans indicate a profound hypolipidemic effect of fish oil, especially lowering of plasma triacylglycerol. Both very-low-density lipoprotein production and apolipoprotein B synthesis are inhibited by fish oil. Finally, fish oil has a mild blood pressure-lowering effect in both normal and mildly hypertensive individuals. These composite effects suggest a prominent therapeutic role for fish oil in the prevention and treatment of coronary artery disease.

Morris MC, Sacks F, Rosner B.
Does fish oil lower blood pressure? A meta-analysis of controlled trials.
Circulation 1993 Aug;88(2):523-33
BACKGROUND. In a meta-analysis of 31 placebo-controlled trials on 1356 subjects, we examined the effect of omega-3 fatty acids in fish oil on blood pressure by grouping studies that were similar in fish oil dose, length of treatment, health of the subjects, or study design. METHODS AND RESULTS. The mean reduction in blood pressure caused by fish oil for the 31 studies was -3.0/-1.5 mm Hg (95% confidence intervals: systolic blood pressure: -4.5, -1.5; diastolic blood pressure: -2.2, -0.8). There was a statistically significant dose-response effect when studies were grouped by omega-3 fatty acid dose: -1.3/-0.7 mm Hg at doses < or = 3 g/d, -2.9/-1.6 mm Hg at 3.3 to 7 g/d, and -8.1/-5.8 mm Hg at 15 g/d. Both eicosapentaenoic acid and docosahexaenoic acid were significantly related to blood pressure response. There was no effect on blood pressure in eight studies of "healthy" persons (mean reduction, -0.4/-0.7 mm Hg) at an overall mean dose of 4.2 g omega-3 fatty acids/d. By contrast, there was a significant effect of -3.4/-2.0 mm Hg in the group of hypertensive studies with a mean fish oil dose of 5.6 g/d and on systolic blood pressure only in six studies of hypercholesterolemic patients (-4.4/-1.1 mm Hg) with a mean dose of 4.0 g/d. A nonsignificant decrease in blood pressure was observed in four studies of patients with atherosclerotic cardiovascular disease (-6.3/-2.9 mm Hg). Variations in the length of treatment (from 3 to 24 weeks), type of placebo, and study design (crossover or parallel groups) did not appear to account for inconsistent findings among studies. CONCLUSIONS. There is a dose-response effect of fish oil on blood pressure of -0.66/-0.35 mm Hg/g omega-3 fatty acids. The hypotensive effect may be strongest in hypertensive subjects and those with clinical atherosclerotic disease or hypercholesterolemia.
Apparent partial remission of breast cancer in 'high risk' patients supplemented with nutritional antioxidants, essential fatty acids and coenzyme Q10.

Mol Aspects Med 1994;15 Suppl:s231-40

Thirty-two typical patients with breast cancer, aged 32-81 years and classified 'high risk' because of tumor spread to the lymph nodes in the axilla, were studied for 18 months following an Adjuvant Nutritional Intervention in Cancer protocol (ANICA protocol). The nutritional protocol was added to the surgical and therapeutic treatment of breast cancer, as required by regulations in Denmark. The added treatment was a combination of nutritional antioxidants (Vitamin C: 2850 mg, Vitamin E: 2500 iu, beta-carotene 32.5 iu, selenium 387 micrograms plus secondary vitamins and minerals), essential fatty acids (1.2 g gamma linolenic acid and 3.5 g n-3 fatty acids) and Coenzyme Q10 (90 mg per day). The ANICA protocol is based on the concept of testing the synergistic effect of those categories of nutritional supplements, including vitamin Q10, previously having shown deficiency and/or therapeutic value as single elements in diverse forms of cancer, as cancer may be synergistically related to diverse biochemical dysfunctions and vitamin deficiencies. Biochemical markers, clinical condition, tumor spread, quality of life parameters and survival were followed during the trial. Compliance was excellent. The main observations were: (1) none of the patients died during the study period. (the expected number was four.) (2) none of the patients showed signs of further distant metastases. (3) quality of life was improved (no weight loss, reduced use of pain killers). (4) six patients showed apparent partial remission.

In a randomized, placebo-controlled trial, the effects of treatment with fish oil (eicosapentaenoic acid, 1.08 g/day) and mustard oil (alpha-linolenic acid, 2.9 g/day) were compared for 1 year in the management of 122 patients (fish oil, group A), 120 patients (mustard oil, group B), and 118 patients (placebo, group C) with suspected acute myocardial infarction (AMI). Treatments were administered about (mean) 18 hours after the symptoms of AMI in all three groups. The extent of cardiac disease, rise in cardiac enzymes, and lipid peroxides were comparable among the groups at entry into the study. After 1 year total cardiac events were significantly less in the fish oil and mustard oil groups compared with the placebo group (24.5% and 28% vs. 34.7%, p < 0.01). Nonfatal infarctions were also significantly less in the fish oil and mustard oil groups compared with the placebo group (13.0% and 15.0% vs. 25.4%, p < 0.05). Total cardiac deaths showed no significant reduction in the mustard oil group; however, the fish oil group had significantly less cardiac deaths compared with the placebo group (11.4% vs. 22.0%, p < 0.05). Apart from the decrease in the cardiac event rate, the fish oil and mustard oil groups also showed a significant reduction in total cardiac arrhythmias, left ventricular enlargement, and angina pectoris compared with the placebo group. Reductions in blood lipoproteins in the two intervention groups were modest and do not appear to be the cause of the benefit in the two groups. Diene conjugates showed a significant reduction in the fish oil and mustard oil groups, indicating that a part of the benefit may be caused by the reduction in oxidative stress. The findings of this study suggest that fish oil and mustard oil, possibly due to the presence of n-3 fatty acids, may provide rapid protective effects in patients with AMI. However, a large study is necessary to confirm this suggestion.

No authors listed


BACKGROUND: There is conflicting evidence on the benefits of foods rich in vitamin E (alpha-tocopherol), n-3 polyunsaturated fatty acids (PUFA), and their pharmacological substitutes. We investigated the effects of these substances as supplements in patients who had myocardial infarction.

METHODS: From October, 1993, to September, 1995, 11,324 patients surviving recent (< or = 3 months) myocardial infarction were randomly assigned supplements of n-3 PUFA (1 g daily, n=2836), vitamin E (300 mg daily, n=2830), both (n=2830), or none (control, n=2828) for 3.5 years. The primary combined efficacy endpoint was death, non-fatal myocardial infarction, and stroke. Intention-to-treat analyses were done according to a factorial design (two-way) and by treatment group (four-way).

FINDINGS: Treatment with n-3 PUFA, but not vitamin E, significantly lowered the risk of the primary endpoint (relative-risk decrease 10% [95% CI 1-18] by two-way analysis, 15% [2-26] by four-way analysis). Benefit was attributable to a decrease in the risk of death (14% [3-24] two-way, 20% [6-33] four-way) and cardiovascular death (17% [3-29] two-way, 30% [13-44] four-way). The effect of the combined treatment was similar to that for n-3 PUFA for the primary endpoint (14% [1-26]) and for fatal events (20% [5-33]). INTERPRETATION: Dietary supplementation with n-3 PUFA led to a clinically important and statistically significant benefit. Vitamin E had no benefit. Its effects on fatal cardiovascular events require further exploration.
Psoriasis vulgaris

Gil A.
Polyunsaturated fatty acids and inflammatory diseases.

Inflammation is overall a protective response, whose main goal is to liberate the human being of cellular lesions caused by micro-organisms, toxins, allergens, etc., as well as its consequences, and of death cells and necrotic tissues. Chronic inflammation, which is detrimental to tissues, is the basic pathogenic mechanism of hypersensitivity reactions against xenobiotics. Other frequent pathologies, for instance atherosclerosis, chronic hepatitis, inflammatory bowel disease (IBD), liver cirrhosis, lung fibrosis, psoriasis, and rheumatoid arthritis are also chronic inflammatory diseases. Chemical mediators of inflammation are derived from blood plasma or different cell-type activity. Biogenic amines, eicosanoids and cytokines are within the most important mediators of inflammatory processes. The different activities of eicosanoids derived from arachidonic acid (20:4 n-6) versus those derived from eicosapentaenoic acid (20:5 n-3) are one of the most important mechanisms to explain why n-3, or omega-3, polyunsaturated fatty acids (PUFA) exhibit anti-inflammatory properties in many inflammatory diseases. Dietary supplements ranging 1-8 g per day of n-3 PUFA have been reportedly beneficial in the treatment of IBD, eczema, psoriasis and rheumatoid arthritis. In addition, recent experimental studies in rats with experimental ulcerative colitis, induced by intrarectal injection of trinitrobenzene sulphonic acid, have documented that treatment with n-3 long-chain PUFA reduces mucosal damage as assessed by biochemical and histological markers of inflammation. Moreover, the defence antioxidant system in this model is enhanced in treated animals, provided that the n-3 PUFA supply is adequately preserved from oxidation.

Soyland E, Lea T, Sandstad B, Drevon A.
Dietary supplementation with very long-chain n-3 fatty acids in man decreases expression of the interleukin-2 receptor (CD25) on mitogen-stimulated lymphocytes from patients with inflammatory skin diseases.

T-cell activation and cytokine production play an important role in several chronic inflammatory diseases. Because n-3 fatty acids exert beneficial effects on the clinical state of some of these diseases, we examined the effect of dietary supplementation of n-3 fatty acids on T-cell proliferation, expression of CD25 (interleukin-2 receptor alpha-chain), secretion of interleukin-2, interleukin-6 and tumour necrosis factor from T-cells from patients with psoriasis and atopic dermatitis. During 4 months, 21 patients supplied 6 g of highly concentrated ethyl esters of EPA and DHA in gelatin capsules daily to their diet. In the control group 20 patients supplied 6 g per day of corn oil in gelatin capsules to their diet. Eicosapentaenoic acid (20:5, n-3) of serum phospholipids increased from 14 (min 4-max 42) to 81 (min 59-max 144) mg l-1 (P < 0.01) in patients with atopic dermatitis receiving n-3 fatty acids, and from 25 (min 7-max 66) to 74 (min 46-max 142) mg l-1 (P < 0.01) in patients with psoriasis, whereas docosahexaenoic acid (22:6, n-3) increased from 65 (min 46-max 120) to 92 (min 54-max 121) mg l-1 (P < 0.05) and from 81 (min 38-max 122) to 92 (min 63-max 169) mg l-1 (NS) in atopic and psoriatic patients, respectively. The changes in the serum phospholipid fatty acid profile in the groups receiving n-3 fatty acids, correlate to the dietary intake of corresponding fatty acids.(ABSTRACT TRUNCATED AT 250 WORDS)

Omega-3 fatty acid-based lipid infusion in patients with chronic plaque psoriasis: results of a double-blind, randomized, placebo-controlled, multicenter trial.

BACKGROUND: Profound changes in the metabolism of eicosanoids with increased concentrations of free arachidonic acid (AA) and its proinflammatory metabolites have been observed in psoriatic lesions. Free eicosapentaenoic acid (EPA) may compete with liberated AA and result in an antiinflammatory effect. OBJECTIVE: Our purpose was to assess the efficacy and safety of intravenously administered fish-oil-derived lipid emulsion on chronic plaque-type psoriasis. METHODS: A double-blind, randomized, parallel group study was performed in eight European centers. Eighty-three patients hospitalized for chronic plaque-type psoriasis with a severity score of at least 15 according to the Psoriasis Area and Severity Index (PASI) participated in a 14-day trial. They were randomly allocated to receive daily infusions with either a omega-3 fatty acid-based lipid emulsion (Omegavenous; 200 ml/day with 4.2 gm of both EPA and docosahexaenoic acid (DHA); 43 patients) or a conventional omega-6-lipid emulsion (Lipovenous; EPA+DHA < 0.1 gm/100 ml; 40
patients). The groups were well matched with respect to demographic data and psoriasis-specific medical history. Efficacy of therapy was evaluated by changes in PASI, in an overall assessment of psoriasis by the investigator, and a self-assessment by the patient. In one center neutrophil 4- versus 5-series leukotriene (LT) generation and platelet 2- versus 3- thromboxane generation were investigated and plasma-free fatty acids were determined. RESULTS: The total PASI score decreased by 11.2 +/- 9.8 in the omega-3 group and by 7.5 +/- 8.8 in the omega-6 group (p = 0.048). In addition, the omega-3 group was superior to the omega-6 group with respect to change in severity of psoriasis per body area, change in overall erythema, overall scaling and overall infiltration, as well as change in overall assessment by the investigator and self-assessment by the patient. Response (defined as decrease in total PASI of at least 50% between admission and last value) was seen in 16 of 43 patients (37%) receiving the omega-3 emulsion and 9 of 40 patients (23%) receiving omega-6 fatty acid-based lipid emulsion. No serious side effects were observed. Within the first few days of omega-3 lipid administration, but not in the omega-6 supplemented patients, a manifold increase in plasma-free EPA concentration, neutrophil leukotriene B5 and platelet thromboxane B3 generation occurred. CONCLUSION: Intravenous omega-3 fatty acid administration is effective in the treatment of chronic plaque-type psoriasis. This effect may be related to changes in inflammatory eicosanoid generation.

Mayser P, Grimm H, Grimminger F.
n-3 fatty acids in psoriasis.
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Increased concentrations of free arachidonic acid (AA) and its proinflammatory metabolites have been observed in psoriatic lesions. Replacement of arachidonic acid by alternative precursor polyunsaturated fatty acids (PUFA), especially eicosapentaenoic acid (EPA), which can be metabolized via the same enzymatic pathways as AA, might be a therapeutic option in psoriasis. However the results of studies evaluating the therapeutic benefit of dietary fish oil have been conflicting and not clearly dose-dependent. To overcome the slow kinetics and limited availability of oral supplementation, we have performed three studies to assess the efficacy and safety of an intravenously administered fish oil derived lipid emulsion on different forms of psoriasis. Patients received daily infusions of either an n-3 fatty acid-based lipid emulsion (Omegaven) or a conventional n-6 lipid emulsion (Lipoven) in different time and dose regimens. In addition to an overall assessment of the clinical course of psoriasis, EPA- and AA-derived neutrophil 5-lipoxygenase (LO)--products, thromboxane (TX) B2/B3, PAF and plasma free fatty acids were investigated. Treatment with n-3 fatty acids resulted in a considerably higher response rate than infusion of n-6 lipids. A more than 10-fold increase in neutrophil EPA-derived 5-LO product formation was noted in the n-3 group, accompanied by a rapid increase in plasma-free EPA within the first days. In conclusion, intravenous n-3-fatty acid administration causes reduction of psoriasis, which may be related to changes in inflammatory eicosanoid generation. The rapidity of the response to intravenous n-3 lipids exceeds by orders of magnitude the hitherto reported kinetics of improvement of psoriatic lesions upon use of oral supplementation.
**Rheumatoide Arthritis**

Gil A.
Polysaturated fatty acids and inflammatory diseases.

Inflammation is overall a protective response, whose main goal is to liberate the human being of cellular lesions caused by micro-organisms, toxins, allergens, etc., as well as its consequences, and of death cells and necrotic tissues. Chronic inflammation, which is detrimental to tissues, is the basic pathogenic mechanism of hypersensitivity reactions against xenobiotics. Other frequent pathologies, for instance atherosclerosis, chronic hepatitis, inflammatory bowel disease (IBD), liver cirrhosis, lung fibrosis, psoriasis, and rheumatoid arthritis are also chronic inflammatory diseases. Chemical mediators of inflammation are derived from blood plasma or different cell-type activity. Biogenic amines, eicosanoids and cytokines are within the most important mediators of inflammatory processes. The different activities of eicosanoids derived from arachidonic acid (20:4 n-6) versus those derived from eicosapentaenoic acid (20:5 n-3) are one of the most important mechanisms to explain why n-3, or omega-3, polysaturated fatty acids (PUFA) exhibit anti-inflammatory properties in many inflammatory diseases. Dietary supplements ranging 1-8 g per day of n-3 PUFA have been reportedly beneficial in the treatment of IBD, eczema, psoriasis and rheumatoid arthritis. In addition, recent experimental studies in rats with experimental ulcerative colitis, induced by intrarectal injection of trinitrobenzene sulphonic acid, have documented that treatment with n-3 long-chain PUFA reduces mucosal damage as assessed by biochemical and histological markers of inflammation. Moreover, the defence antioxidant system in this model is enhanced in treated animals, provided that the n-3 PUFA supply is adequately preserved from oxidation.

Long-term effect of omega-3 fatty acid supplementation in active rheumatoid arthritis. A 12-month, double-blind, controlled study.

OBJECTIVE. To study the long-term effects of supplementation with omega-3 fatty acids (omega 3) in patients with active rheumatoid arthritis. METHODS. Ninety patients were enrolled in a 12-month, double-blind, randomized study comparing daily supplementations with either 2.6 gm of omega 3, or 1.3 gm of omega 3 + 3 gm of olive oil, or 6 gm of olive oil. RESULTS. Significant improvement in the patient’s global evaluation and in the physician’s assessment of pain was observed only in those taking 2.6 gm/day of omega 3. The proportions of patients who improved and of those who were able to reduce their concomitant antirheumatic medications were significantly greater with 2.6 gm/day of omega 3. CONCLUSION. Daily supplementation with 2.6 gm of omega 3 results in significant clinical benefit and may reduce the need for concomitant antirheumatic medication.

Ariza-Ariza R, Mestanza-Peralta M, Cardiel MH.
Omega-3 fatty acids in rheumatoid arthritis: an overview.

OBJECTIVES: To review background, pharmacological properties, mechanisms of action, and published clinical experience using omega-3 fatty acids in rheumatoid arthritis. MATERIALS AND METHODS: English language publications were identified through a computerized search (using MEDLINE) between 1979 and 1995 using the terms "omega-3 fatty acids" and "fish oil". In addition, manual search and cross references were used to obtain published articles on the subject. Papers showing evidence of pharmacological properties and mechanisms of action were analyzed. For therapeutic efficacy, only randomized clinical trials are presented in this article. All papers were reviewed by a board certified rheumatologist with training in research methodology and critical appraisal skills. He was aware of study objectives. RESULTS: Main results are summarized in the text and presented in tables. Mean change from baseline is presented only for patients treated with omega-3 fatty acids. Omega-3 fatty acids are superior with respect to placebo in improving some outcome measures, and decrease the long-term requirements for nonsteroidal antiinflammatory drugs. Some of these effects are statistically significant, but their clinical significance remain to be established. CONCLUSIONS: Treatment with omega-3 fatty acids has been associated with improvement in some outcome measures in rheumatoid arthritis. Studies are needed to determine if they might represent an alternative to nonsteroidal antiinflammatory drugs in certain circumstances.

Kremer JM.
n-3 fatty acid supplements in rheumatoid arthritis.
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Ingestion of dietary supplements of n-3 fatty acids has been consistently shown to reduce both the number of tender joints on physical examination and the amount of morning stiffness in patients with rheumatoid arthritis. In these cases, supplements were consumed daily in addition to background medications and the clinical benefits of the n-3 fatty acids were not apparent until they were consumed for \( \geq 12 \) wk. It appears that a minimum daily dose of 3 g eicosapentaenoic and docosahexaenoic acids is necessary to derive the expected benefits. These doses of n-3 fatty acids are associated with significant reductions in the release of leukotriene B\( (4) \) from stimulated neutrophils and of interleukin 1 from monocytes. Both of these mediators of inflammation are thought to contribute to the inflammatory events that occur in the rheumatoid arthritis disease process. Several investigators have reported that rheumatoid arthritis patients consuming n-3 dietary supplements were able to lower or discontinue their background doses of nonsteroidal antiinflammatory drugs or disease-modifying antirheumatic drugs. Because the methods used to determine whether patients taking n-3 supplements can discontinue taking these agents are variable, confirmatory and definitive studies are needed to settle this issue. n-3 Fatty acids have virtually no reported serious toxicity in the dose range used in rheumatoid arthritis and are generally very well tolerated.


Rheumatoid arthritis (RA) is a debilitating disease and is associated with increased risk of cardiovascular disease and osteoporosis. Poor nutrient status in RA patients has been reported and some drug therapies, such as nonsteroidal anti-inflammatory drugs (NSAIDs), prescribed to alleviate RA symptoms, may increase the requirement for some nutrients and reduce their absorption. This paper reviews the scientific evidence for the role of diet and nutrient supplementation in the management of RA, by alleviating symptoms, decreasing progression of the disease or by reducing the reliance on, or combating the side-effects of, NSAIDs. Supplementation with long-chain n-3 polyunsaturated fatty acids (PUFA) consistently demonstrates an improvement in symptoms and a reduction in NSAID usage. Evidence relating to other fatty acids, antioxidants, zinc, iron, folate, other B vitamins, calcium, vitamin D and fluoride are also considered. The present evidence suggests that RA patients should consume a balanced diet rich in long-chain n-3 PUFA and antioxidants. More randomized long-term studies are needed to provide evidence for the benefits of specific nutritional supplementation and to determine optimum intake, particularly for n-3 PUFA and antioxidants.
Polyunsaturated fatty acid (fish or evening primrose oil) for schizophrenia.

Cochrane Database Syst Rev 2000:CD001257

BACKGROUND: Limited evidence gives support to an hypothesis suggesting that the symptoms of schizophrenia may result from altered neuronal membrane structure and metabolism. The latter are dependent on blood plasma levels of certain essential fatty acids (EFAs) and their metabolites. Several studies have shown those with schizophrenia often have low levels of the particular EFAs necessary for normal nerve cell membrane metabolism. OBJECTIVES: To review the effects of supplementing standard antipsychotic treatment with polyunsaturated fatty acids, whether essential (EFAs) or non-essential, for those with schizophrenia and, in recent updates to also evaluate the effects of EFA's as a sole antipsychotic treatment. To evaluate the relative efficacy of different types of fatty acid supplementation. SEARCH STRATEGY: Relevant randomised trials were identified by searching the following electronic databases: Biological Abstracts (1985-1998), CINAHL (1982-1998), Cochrane Library (Issue 4, 1999), Cochrane Schizophrenia Group's Register (February 2000), EMBASE (1980-1998), MEDLINE (1966-1998) and PsycLIT (1974-1998). In addition, reviewers searched references of included and excluded studies and contacted authors to identify further studies. SELECTION CRITERIA: All randomised clinical trials of polyunsaturated fatty acid supplementation to standard treatment or as primary intervention for schizophrenia (however defined) versus standard care. DATA COLLECTION AND ANALYSIS: Reviewers evaluated data independently and analysed on an intention-to-treat basis. They assumed that people who left the study early or were lost to follow-up had no improvement. Where possible and appropriate relative risk (RR) and their 95% confidence intervals (CI) were calculated. The number needed to treat (NNT) was estimated. For continuous data weighted mean differences (WMD) and their 95% confidence intervals were calculated. Data were inspected for heterogeneity and publication biases. MAIN RESULTS: Four relatively small trials (total n=204) showed low levels of loss to follow up and adverse effects for those taking essential fatty acids. Early results from a few trials suggest a positive effect of eicosapentaenoic acid (EPA) over placebo for scale-derived mental state outcomes. The data, however, is limited making these results difficult to analyse and interpret with confidence. A single small study (n=30) investigated the value of using EPA as sole treatment for people hospitalised for relapse. Results suggest that EPA may help one third of people avoid instigation of standard antipsychotic drugs for 12 weeks (RR 0.6, CI 0.4-0.91). There were no clear effects of primrose oil (omega-6) EFA supplementation. REVIEWER'S CONCLUSIONS: All data are preliminary, but results look encouraging for fish oil. EPA does not seem harmful, may be acceptable to people with schizophrenia and have moderately positive effect. A further trial is soon to be reported from the USA and more are underway or planned in the South Africa and Norway. Considering that EPA may be an acceptable intervention, large, long simple studies reporting clinically meaningful data should be anticipated.