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The Effects of Fish Oil and Marine Omega-3 Fatty Acids on Human Health- a Review Article

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Abstract: Eating fatty fish and marine omega-3 fatty acids, which are found in fish oil, seems to protect men from heart failure according to one of the largest studies to investigate the association. However, the effect was seen only in men who eat approximately one serving of fatty fish a week and who had a moderate intake of marine omega-3 fatty acids (approximately 0.3 grams a day). Eating more did not give a greater benefit and, in fact, returned the chances of heart failure to the same level as that seen in men who never consume fatty fish or fish oils.

Key words: Fish Oil, Omega-3 fatty acids, Health benefits.

INTRODUCTION

Scientific publications praising the merits of omega-3 have reached an astronomical figure. Most people today no longer know where to turn amid this wealth of information. In this article I will present some key facts which can provide a better understanding of the omega-3 fatty acids. Fish oils, due to their nature, are the most highly, overly refined and processed so-called "natural foods". This article will not focus on the benefits of omega-3 fatty acids for that information can be found in a variety of publications. This article will address the question of, what is really natural about omega-3 fatty acids from fish oil and how to improve the bioavailability and where to find an all-natural whole food omega-3 fatty acid. EPA and DHA are mainly present in seafood (fish oil) and to a lesser degree in meat. However, meat is higher in omega-6 versus omega-3. The presence of omega-3 fatty acids in animals is a direct result of their plant diet. In fact, in the case of fish, it is the one-celled marine organisms like algae or plankton which synthesize EPA and DHA. Their consumption by crustaceans and fish permits an accumulation of omega-3 fatty acid in the tissue of predatory animals. As a general rule, the fattier a fish is (5% or more lipids) the higher its level of omega-3 fatty acids. Among them, salmon, herring, eel, mackerel, sardine and trout are good sources of omega-3 fatty acids. Certain crustaceans are also rich in omega-3's including krill, but they are also high in cholesterol and the cholesterol is only removed by the use of hexane. As an example, a 100 gram serving of Atlantic salmon provides about 1.2 grams of omega-3 fatty acids, but several factors influence omega-3 content; geographic origin, species, diet and age. Interestingly, farmed Atlantic salmon is generally fattier than wild salmon and thus richer in EPA and DHA (+15% on average). Added to this is a difference in maturity between these two types of salmon. The slow growth of wild salmon increases the risks of absorption and storage of heavy metals in their tissues, unlike farm salmon which grow more quickly. In spite of the disparities in sources of omega-3's, it's important to consume one serving of fish, preferably fatty fish, at least once weekly in order to cover in part the EPA and DHA requirements. For those who may not have the means or the desire to eat fish several times a week, can find a more reasonable solution by selecting Vectomega, a natural whole food omega-3 fatty acid supplement in the preferred form and ratio of EPA and DHA [1,2].

Some Facts about Treatment with Omega-3 Fatty Acids:

- Fish oil is currently the recommended source of omega-3. Flaxseed oil and perilla oil contain a different type of omega-3. Several cases of hypomania have occurred in people taking flaxseed oil, but the causes remain unclear.

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- Omega-3s are usually added to whatever treatment you are already receiving, there is not yet enough experience to recommend using them alone in most cases. There are no known interactions with psychotropic drugs.
- Always discuss the use of any new medications, over-the-counter or otherwise, with your prescriber. Drug interaction risks and other dangers can be associated with any biological treatment.
- A starting dose of 5 grams of omega-3 per day is currently recommended. Calculate dosage based on the concentration of omega-3 fatty acids listed on the label of the fish oil supplement. This can be confusing due to the variety of different preparations. Focus on the omega-3 concentration in each capsule.
- The 2 main omega-3 fatty acids in fish oil are EPA and DHA. A high ratio of EPA to DHA is desirable in a fish oil capsule. Other desirable characteristics include small capsule size and high omega-3 concentration, which minimizes the number of capsules required per day.
- Dosage can be split between morning and night or taken all at night.
- Due to the volume of fish required to achieve the recommended daily dosage, it is not recommended that you use eating fish alone as a means of getting your Omega-3s.
- You may experience some fishy taste but treatment with fish oil does not make you smell like fish! Taking the supplements with orange juice can reduce the fishy taste.
- Do not pursue this treatment if you are taking any type of blood thinners, even high doses of aspirin, or any medications or substances that have the same blood thinning effect.
- Do not use cod liver or other fish liver oils to achieve high omega-3 doses, since it could result in vitamin A toxicity.
- The omega-3 fatty acids are not a panacea, but in many cases they do appear to be as effective as conventional medications [3,4].

Some Additional Facts about Omega-3 Fatty Acids:

- Cold-water, oily fish are the main source of marine-derived omega-3 fatty acids.
- Farm-raised fish that are fed grain alone may contain little or no Omega-3s. Omega-3s come from algae that, in the marine food chain, are then eaten by krill who are in turn eaten by larger fish.
- Omega-3s have numerous health benefits in other areas, including heart, cholesterol, rheumatoid arthritis, & Crohn's Disease, to name a few. Again our thanks to Dr. Stoll for letting us share this information from his findings. A new web site has been launched by Dr. Stoll and other practitioners that contains information on where you can order a special Omega 3 formulation designed to maximize its efficacy [3].

Fish Consumption, Fish Oil, Omega-3 Fatty Acids and Cardiovascular Disease: Since the first AHA Science Advisory "Fish Consumption, Fish Oil, Lipids and Coronary Heart Disease" [1], important new findings, including evidence from randomized controlled trials (RCTs), have been reported about the beneficial effects of omega-3 (or n-3) fatty acids on cardiovascular disease (CVD) in patients with preexisting CVD as well as in healthy individuals [2]. New information about how omega-3 fatty acids affect cardiac function (including antiarrhythmic effects), hemodynamics (cardiac mechanics) and arterial endothelial function have helped clarify potential mechanisms of action. The present Statement will address distinctions between plant-derived (α-linolenic acid, C18:3n-3) and marine-derived (eicosapentaenoic acid, C20:5n-3 [EPA] and docosahexaenoic acid, C22:6n-3 [DHA]) omega-3 fatty acids. (Unless otherwise noted, the term omega-3 fatty acids will refer to the latter.) Evidence from epidemiological studies and RCTs will be reviewed and recommendations reflecting the current state of knowledge will be made with regard to both fish consumption and omega-3 fatty acid (plant- and marine-derived) supplementation. This will be done in the context of recent guidance issued by the US Environmental Protection Agency and the Food and Drug Administration (FDA) about the presence of environmental contaminants in certain species of fish.

Coronary Heart Disease: Fish consumption has been shown to be related to reduced sudden cardiac death. In a population-based, nested, case-control study, a strong negative relationship was reported between fish intake and risk for sudden death (ie, 5.5 g of omega-3 fatty acids per month, equivalent to two fatty fish meals per week, was associated with a 50% reduced risk of primary cardiac arrest) [5]. In the US Physicians' Health Study, men who consumed fish at least once weekly had a relative risk of sudden death of 0.48 (P=0.04) versus men who consumed fish less than once per month. [6] A recent report from the Physicians' Albert Study [7] reported an inverse

relationship between blood levels of long-chain omega-3 fatty acids and risk of sudden death in men without a history of CVD. The relative risk of sudden death was significantly lower among men with levels in the third quartile (RR=0.28) and the fourth quartile (RR=0.19) compared with men whose blood levels were in the first quartile.

Further evidence for a protective effect of omega-3 fatty acids comes from two recent studies by Landmark *et al.* [8,9] who reported that chronic intake of fish or fish oil was associated with a reduction in infarct size as estimated by the frequency of Q-wave infarcts and by peak creatine kinase and lactate dehydrogenase activities after MI. In contrast to all the studies demonstrating a beneficial association, the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study found that estimated omega-3 fatty acid intake from fish was associated with a trend toward increased relative risk of coronary death after adjustment for trans, saturated and cis-monounsaturated fatty acids [10].

Triglycerides: The hypotriglyceridemic effects of omega-3 fatty acids from fish oils are well established. In a comprehensive review of human studies, Harris [11] reported that ≈4 g/d of omega-3 fatty acids from fish oil decreased serum triglyceride concentrations by 25% to 30%, with accompanying increases in LDL cholesterol of 5% to 10% and in HDL cholesterol of 1% to 3%. A dose-response relationship exists between omega-3 fatty acid intake and triglyceride lowering [11]. Postprandial triglyceridemia is especially sensitive to chronic omega-3 fatty acid consumption, [12,13] with quite small intakes (<2 g/d) producing significant reductions [14]. The plasma lipid and lipoprotein responses to fish oil are comparable in diabetic and nondiabetic subjects [15]. In addition, a recent meta-analysis of 26 trials of subjects with type 1 or type 2 diabetes mellitus reported no effects of fish oil on hemoglobin A_{1c}, [16] although fasting blood glucose levels rose slightly in the latter group.

Fish oil can have a therapeutic role in the treatment of marked hypertriglyceridemia (>750 mg/dL). Effective doses of omega-3 fatty acids range from 3 to 5 g/d, which can only be obtained consistently by supplementation. At present, it seems that both EPA and DHA have triglyceride-lowering properties [17]. Patients taking >3 g of EPA+DHA from supplements should do so only under a physician's care because the FDA has noted that an intake in excess of this level could result in excessive bleeding in some individuals [18]. In contrast, cardioprotective intakes seem to be considerably lower (≈1 g/d), have almost no potential for adverse effects and can be achieved by diet.

Blood Pressure: Omega-3 fatty acids seem to have a small, dose-dependent, hypotensive effect, the extent of which seems to be dependent on the degree of hypertension [19]. In a meta-analysis, Morris *et al.* [20] found a significant reduction in blood pressure of -3.4/-2.0 mm Hg in studies with hypertensive subjects who consumed 5.6 g/d of omega-3 fatty acids. Likewise, *Appel et al.* [21] found that blood pressure was decreased -5.5/-3.5 mm Hg in trials of untreated hypertensives given >3 g/d of omega-3 fatty acids. DHA seems to be more effective than EPA in lowering blood pressure [22]. Still, in view of the high dose required to lower blood pressure and the proven efficacy of other nutritional factors and of antihypertensive medications, an increased intake of omega-3 fatty acids has a limited role in the management of hypertension.

Thrombosis and Hemostasis: Omega-3 fatty acids decrease platelet aggregation [23,24] resulting in a modest prolongation of bleeding times (reviewed by Knapp [25]). Some evidence indicates that fish oil supplementation may enhance fibrinolysis [26]. Although omega-3 fatty acid intake has been negatively associated with levels of fibrinogen, Factor VIII and von Willebrand factor [27] more recent evidence from the Coronary Artery Risk Development In young Adults (CARDIA) study found no significant associations between customary intakes of fish (4 to 39 g/d) and omega-3 fatty acids (0.9 to 4.1 g/d) and these coagulation factors [28]. Marckmann *et al.* [29] also found no effect of omega-3 fatty acids (0.9 g/d) on levels of Factor VII, fibrinogen, endogenous fibrinolysis, ß-thromboglobulin and von Willebrand factor. In contrast, a recent study reported that coronary patients taking 5.1 g/d of omega-3 fatty acids for 6 months experienced a reduction in von Willebrand factor (128% versus 147% for controls) and thrombomodulin (25 versus 33 ng/mL) [30]. Although it seems clear that omega-3 fatty acids beneficially influence collagen-induced platelet aggregation (thereby affecting hemostasis), their effects on thrombosis remain unclear. There is little evidence to suggest that an intake <3 g/d of omega-3 fatty acids would cause clinically significant bleeding.

Arrhythmias: The possibility that omega-3 fatty acids (including α-linolenic acid) may reduce risk for sudden cardiac death is based on evidence from a prospective cohort study, a case-control study and four prospective dietary intervention trials [31-34]. Proposed mechanisms to explain these observations center not on lipid or blood pressure lowering or on antithrombotic effects, but on a novel stabilizing effect of omega-3 fatty acids on the myocardium itself. Evidence for a direct effect of these

fatty acids on the heart has come from several observations. First, increased heart rate variability in survivors of MI was associated with the consumption of one fish meal per week or fish oil supplements (4.3 g/d of omega-3 fatty acids) [35]. Increases in this parameter predict a lower risk of mortality due to arrhythmic events in post-MI patients. EPA and DHA also have been shown to reduce resting heart rate and increase left ventricular filling capacity. Animal experiments and cell culture studies have shown that fish oil has potent antiarrhythmic effects. For example, studies with rats [36] and dogs [37,38] have shown that pretreatment with omega-3 fatty acids reduced damage to cardiac tissue and forestalled the development of ventricular dysrhythmias when heart attacks were induced. Similar observations were made in fish oil-fed cats that were protected from cerebral damage after stroke induction [39]. *In vitro* induction of tachyarrhythmias in cultured neonatal rat ventricular myocytes by various pharmacological agents (such as ouabain) can be prevented or abolished by the addition of omega-3 fatty acids to the culture medium (reviewed by Kang and Leaf. This seems to be due to the ability of omega-3 fatty acids to prevent calcium overload by maintaining the activity of L-type calcium channels during periods of stress and to increase the activity of cardiac microsomal Ca^{2+}/Mg^{2+}-ATPase. In addition, omega-3 fatty acids (including α-linolenic acid) are potent inhibitors of voltage-gated sodium channels in cultured neonatal cardiac myocytes, which may contribute to the reduction in arrhythmia [40].

Other Biological Effects: Mechanisms to explain the antiatherogenic (inhibition of new plaque development) effect of omega-3 fatty acids have recently been proposed. For example, EPA and DHA seem to alter the metabolism of adhesion molecules such as vascular cell adhesion molecule-1 (VCAM-1), E-selectin and intercellular adhesion molecule-1 (ICAM-1). There is also in vitro evidence that DHA reduces endothelial expression of VCAM-1 and the expression of E-selectin, ICAM-1, interleukin (IL)-6 and IL-8 in stimulated cells [41]. On the other hand, a study in male smokers with hyperlipidemia showed that six weeks of omega-3 fatty acid supplementation (4.8 g/d) increased soluble forms of E-selectin and VCAM-1. A subsequent study in coronary patients given supplemental omega-3 fatty acids (5.1 g/d for 6 months) found similar results. Fish oil also affects the metabolism of inflammatory mediators like the interleukins and tumor necrosis factor-α, molecules also believed to play a role in atherogenesis and plaque stability [42].

REFERENCES

1. Brude, I.R., C.A., Drevon and I. Hjermann, 1997 Peroxidation of LDL from combined-hyperlipidemic male smokers supplied with omega-3 fatty acids and antioxidants. Arterio Thromb Vasc Biol., 17: 2576-2588. Follow this style in all references.
2. Kris-Etherton, P.M., D.S. Taylor and S. Yu-Poth 2000. Polyunsaturated fatty acids in the food chain in the United States. Am. J. Clin Nutr., 71(1 Suppl): 179S-188S.
3. Endres, S., Von and C. Schacky, 1996. n-3 polyunsaturated fatty acids and human cytokine synthesis. Curr Opin Lipidol., 7: 48-52.
4. Sorensen, N.S., P. Marckmann and C.E. Hoy, 1998. Effect of fish-oil-enriched margarine on plasma lipids, low-density-lipoprotein particle composition, size and susceptibility to oxidation. Am. J. Clin Nutr., 68: 235-241.
5. Siscovick, D.S., T.E., Raghunathan and I. King, 1995. Dietary intake and cell membrane levels of long-chain n-3 polyunsaturated fatty acids and the risk of primary cardiac arrest. JAMA., 274: 1363-1367.
6. Christensen, J.H., E. Korup and J. Aaroe, 1997. Fish consumption, n-3 fatty acids in cell membranes and heart rate variability in survivors of myocardial infarction w ith left ventricular dysfunction. Am. J. Cardiol., 79: 1670-1673.
7. Albert, C.M., H. Campos and M.J. Stampfer, 2002. Blood levels of long-chain n-3 fatty acids and the risk of sudden death. N Engl. J. Med., 346: 1113-1118.
8. Landmark, K., M. Abdelnoor and B. Kilhovd, 1998. Eating fish may reduce infarct size and the occurrence of Q wave infarcts. Eur. J. Clin Nutr., 52: 40-44.
9. Landmark, K., M., Abdelnoor and P. Urdal, 1998. Use of fish oils appears to reduce infarct size as estimated from peak creatine kinase and lactate dehydrogenase activities. Cardiol., 89: 94-102.
10. Pietinen, P., A., Ascherio and P. Korhonen, 1997. Intake of fatty acids and risk of coronary heart disease in a cohort of Finnish men: the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. Am. J. Epidemiol., 145: 876-887.
11. Harris, W.S., 1997. n-3 Fatty acids and serum lipoproteins: human studies. Am. J. Clin Nutr., 65(5 Suppl): 1645S-1654S.
12. Sanders, T.A., F.R. Oakley and G.J. Miller, 1997. Influence of n-6 versus n-3 polyunsaturated fatty acids in diets low in saturated fatty acids on plasma lipoproteins and hemostatic factors. Arterioscler Thromb Vasc Biol., 17: 3449-3460.

13. Harris, W.S., W.E., Connor and N. Alam, 1988. Reduction of postprandial triglyceridemia in humans by dietary n-3 fatty acids. J. Lipid Res., 29: 1451-1460.
14. Roche, H.M. and M.J. Gibney, 1996. Postprandial triacylglycerolaemia: the effect of low-fat dietary treatment with and without fish oil supplementation. Eur. J. Clin Nutr., 50: 617-624.
15. Montori, V.M., A. Farmer and P.C. Wollan, 2000. Fish oil supplementation in type 2 diabetes: a quantitative systematic review. Diabetes Care, 23: 1407-1415.
16. Friedberg, C.E., M.J. Janssen and R.J. Heine, 1998. Fish oil and glycemic control in diabetes: a meta-analysis. Diabetes Care, 21: 494-500.
17. Grimsgaard, S., K.H. Bonaa and J.B. Hansen, 1997. Highly purified eicosapentaenoic acid and docosahexaenoic acid in humans have similar triacylglycerol-lowering effects but divergent effects on serum fatty acids. Am. J. Clin Nutr., 66: 649-659.
18. Uauy, R. and P. Mena, 1999. Valenzuela A. Essential fatty acids as determinants of lipid requirements in infants, children and adults. Eur. J. Clin Nutr., 53(Suppl 1): S66-S77.
19. Howe, P.R., 1997. Dietary fats and hypertension: focus on fish oil. Ann. N Y Acad Sci., 827: 339-352.
20. Morris, M.C., F. Sacks and B. Rosner, 1993. Does fish oil lower blood pressure? A meta-analysis of controlled trials. Circulation, 88: 523-533.
21. Appel, L.J., E.R. Miller and AJ. Seidler, 1993. Does supplementation of diet with 'fish oil' reduce blood pressure? A meta-analysis of controlled clinical trials. Arch Intern Med., 153: 1429-1438.
22. Mori, T.A., G.F. Watts and V. Burke, 2000. Differential effects of eicosapentaenoic acid and docosahexaenoic acid on vascular reactivity of the forearm microcirculation in hyperlipidemic, overweight men. Circulation, 102: 1264-1269.
23. Agren, J.J., S. Vaisanen and O. Hanninen, 1997. Hemostatic factors and platelet aggregation after a fish-enriched diet or fish oil or docosahexaenoic acid supplementation. Prostaglandins Leukot Essent Fatty Acids., 57: 419-421.
24. Mori, T.A., L.J. Beilin and V. Burke, 1997. Interactions between dietary fat, fish and fish oils and their effects on platelet function in men at risk of cardiovascular disease. Arterioscler Thromb Vasc Biol., 17: 279-286.
25. Knapp, H.R., 1997. Dietary fatty acids in human thrombosis and hemostasis. Am. J. Clin Nutr., 65(5 Suppl): 1687S-1698S.
26. Barcelli, U., P. Glas-Greenwalt and V.E. Pollak, 1985. Enhancing effect of dietary supplementation with omega-3 fatty acids on plasma fibrinolysis in normal subjects. Thromb Res., 39: 307-312.
27. Shahar, E., A.R., Folsom and K.K. Wu, 1993. Associations of fish intake and dietary n-3 polyunsaturated fatty acids with a hypocoagulable profile. The Atherosclerosis Risk in Communities (ARIC) Study. Arterioscler Thromb., 13: 1205-1212.
28. Archer, S.L., D. Green and M. Chamberlain, 1998. Association of dietary fish and n-3 fatty acid intake with hemostatic factors in the coronary artery risk development in young adults (CARDIA) study. Arterioscler Thromb Vasc Biol., 18: 1119-1123.
29. Marckmann, P., E.M., Bladbjerg and J. Jespersen, 1997. Dietary fish oil (4 g daily) and cardiovascular risk markers in healthy men. Arterioscler Thromb Vasc Biol., 17: 3384-3391.
30. Johansen, O., I. Seljeflot and A.T. Hostmark, 1999. The effect of supplementation with omega-3 fatty acids on soluble markers of endothelial function in patients with coronary heart disease. Arterioscler Thromb Vas Biol., 19: 1681-1686.
31. Christensen, J.H., P. Gustenhoff and E. Korup, 1996. Effect of fish oil on heart rate variability in survivors of myocardial infarction: a double blind randomised controlled trial. BMJ., 312: 677-678.
32. Billman, G.E. and J.X. Kang, 1997. Leaf A. Prevention of ischemia-induced cardiac sudden death by n-3 polyunsaturated fatty acids in dogs. Lipids., 32: 1161-168.
33. Grimsgaard, S., K.H. Bonaa and J.B. Hansen, 1998. Effects of highly purified eicosapentaenoic acid and docosahexaenoic acid on hemodynamics in humans. Am. J. Clin Nutr., 68: 52-59.
34. Pepe, S. and P.L. McLennan, 1996. Dietary fish oil confers direct antiarrhythmic properties on the myocardium of rats. J. Nutr., 126: 34-42.
35. De Caterina, R. and P. Libby 1996. Control of endothelial leukocyte adhesion molecules by fatty acids. Lipids., 31: S57-S63.
36. Bayon, Y., M. Croset and D. Daveloose, 1995. Effect of specific phospholipid molecular species incorporated in human platelet membranes on thromboxane A_2/prostaglandin H_2 receptors. J. Lipid Res., 36: 47-56.
37. Lee, R.T. and P. Libby, 1997. The unstable atheroma. Arterioscler Thromb Vasc Biol., 17: 1859-1867. 96.

38. Kinoshita, I., K. Itoh and M. Nishida-Nakai, 1994. Antiarrhythmic effects of eicosapentaenoic acid during myocardial infarction–enhanced cardiac microsomal (Ca^{2+}-Mg^{2+})-ATPase activity. Japan Circ J., 58: 903-912. 82.
39. Black, K.L., B. Culp and D. Madison, 1979. The protective effects of dietary fish oil on focal cerebral infarction. Prostaglandins Med., 3: 257-268.
40. Hallaq, H., T.W. Smith and A. Leaf, 1992. Modulation of dihydropyridine-sensitive calcium channels in heart cells by fish oil fatty acids. Proc Natl. Acad. Sci. USA., 89: 1760-1764.
41. Harris, W.S., G.S. Rambjor and S.L. Windsor, 1997. N-3 fatty acids and urinary excretion of nitric oxide metabolites in humans. Am. J. Clin Nutr., 65: 459-464.
42. De Caterina, R., J.K. Liao and P. Libby, 2000. Fatty acid modulation of endothelial activation. Am. J. Clin Nutr., 71(1 Suppl): 213S-223S. 43.