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THE IMPACT OF MARINE N-3 PUFA ON CORONARY HEART DISEASE AND SUDDEN CARDIAC DEATH- REVIEW

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ABSTRACT

Objective: After few reports about protective effect on coronary heart disease, the therapeutic use of n-3 polyunsaturated fatty acid aroused .Many studies and meta-analyses have reported that the risk of Coronary Heart Disease (CHD) and Cardiovascular (CV) death reduced with the intake of fish and n-3 PUFA. n-3 PUFA may also modulate autonomic control of the heart because it's abundant in the brain and other nervous tissue as well as in cardiac tissue. This might explain the protection against sudden cardiac death (SCD) by n-3 PUFA. The pathogenesis of SCD depends upon autonomic nervous system. Heart rate variability (HRV) can be used as marker of autonomic control and low HRV is a predictor for SCD. The studies have demonstrated that supplementation with n-3 PUFA seems to increase HRV which could be explanation for decreased SCD sometimes observed after omega-3 supplementation. We critically reviewed the effect of n-3 PUFA containing diet on coronary heart disease and heart rate variability.

INTRODUCTION

After few reports about protective effect on coronary heart disease, the therapeutic use of n-3 PUFA aroused (Bang and Dyerberg, 1972). Several meta-analyses have reported reduced risk of CV events, due to reduction of CHD and CV death due to fish and n-3 PUFA intake (He *et al*., 2004). Cardiac autonomic control is important in the pathogenesis of SCD. SCD is considered to be controlled with increase in vagal activity (Billman *et al*., 1999) whereas cardiac arrhythmias is seen with sympathetic activity (Task Force of the European Society of Cardiology, 1996). The importance of prevention of SCD depends upon the modulation of autonomic control and change in vagal or sympathetic tone. Omega-3 PUFAs are components of membrane phospholipids throughout the body but particularly docsahexonic acid (DHA) is highly concentrated in the central nervous system. As DHA is also abundant in cardiac tissue it is likely that omega-3 PUFA might modulate autonomic control of the heart. We critically reviewed clinical trial reporting data on the anti-arrhythmic effect of n-3 PUFA in several clinical settings, i.e., patient with CHD (Marchioli, 1999), and at risk of atrial fibrillation (Calo *et al*., 2005).

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PUFAs- Chemistry and origin

Fatty acids (FAs) with atleast two double bond are designated as polyunsaturated. For PUFAs, the position of first double bond from methyl-/(n/omega-) end of the molecule has given rise to the terminology n-3(omega-3) FAs,n-6 FAs and n-9 FAs (Drevon, 1992). n-3 and n-6 PUFAs are not synthesized by human body, so they are suppose to be ingested (Mozaffarian and Wu, 2011). N-3 PUFA with more than 20 carbon atom are made by phytoplankton and mainly ingested from fatty fish and marine animals. The two important marine FAs are eicosapentaenoic acid and docosahexaenoic acid. The main body content of DHA and EPA is dependent on the amount ingested.

The Difference Between Unsaturated and Saturated Fatty Acids

There are fats and fatty acids that can help to lower LDL or bad cholesterol level and improve overall heart health. All fatty acids are made up of a chains of carbon and hydrogen atoms. Saturated fatty acids are saturated with hydrogen atoms meaning that each carbon atom is linked with a hydrogen atoms. Consuming a large amount of saturated fats possess a greater health risks. Saturated fat is linked with high cholesterol and heart disease. Unsaturated fatty acids, on the other hand, have missing hydrogen atoms. Fatty acids with only one pair of missing hydrogen atoms are known as monounsaturated fatty acids. Polyunsaturated fatty acids are

missing more than one pair of hydrogen atoms and replaced by double bonds. (www.fitday.com)

Benefits of PUFAs

Monounsaturated fats are considered the healthiest type of fats. However, PUFA are better than saturated fatty acids. They have shown to reduce LDL or bad cholesterol while increasing HDL or good cholesterol. Polyunsaturated fatty acids contains essential fatty acids (EFAs) like omega-3 and omega-6 acids. These are fatty acids that body needs but cannot produce. EFAs are critical components of cell membrane production. Polyunsaturated fatty acids also regulates the production of prostaglandins, a substance that help the body's inflammatory functions. Another benefit of PUFA is they release a hormone which sends signal to brain when stomach is full. This prevents overeating and can aid in weight loss. When eaten in moderation and as a part of diet high in fibre, they can reduce the risk of heart disease. (www.fitday.com)

Sources of PUFAs

PUFAs can be found in seafood like wild salmon and halibut. Certain vegetable oils are other sources of EFAs. Sunflower-seed, corn, sesame, soy and sunflower oil contains high level of PUFAs. Peanut butter, walnuts, soybeans and grains are other ways to get daily sources of PUFAs. (www.fitday.com)

Coronary Heart Disease

Coronary heart disease (CHD) is a disease in which a waxy substance called plaque (plak) builds up inside the coronary arteries. These arteries supply oxygen-rich blood to heart muscle. When plaque builds up in the arteries, the condition is called atherosclerosis. The buildup of plaque occurs over many years. Over time, plaque can harden or rupture. A large blood clot can mostly or completely block blood flow through a coronary artery. Over time, ruptured plaque also hardens and narrows the coronary arteries. (www.nhlbi.nih.gov/health/health-topics/topics/cad/)

Causes of CHD

Studies suggest that CHD starts when certain factors damage the inner layers of the coronary arteries. These factors include:

1. Smoking
2. High levels of certain fats and cholesterol in the blood
3. High blood pressure
4. High levels of sugar in the blood due to insulin resistance or diabetes
5. Blood vessel inflammation

Plaque might begin to build up where the arteries are damaged. The buildup of plaque in the coronary arteries may start in childhood. Hardened plaque narrows the coronary arteries and reduces the flow of oxygen- rich blood to the heart. This can cause angina. (www.nhlbi.nih.gov/health/health-topics/topics/cad/)

Studies on coronary heart disease and PUFA

The study suggesting an antiarrhythmic effect of n-3 PUFA was the Diet and Reinfarction Trial (DART) study carried out on 1989 (Burr *et al*., 1989). A decreased mortality and sudden death were observed in post-MI patients receiving a Mediterranean alpha-linolenic acid (ALA)-rich diet (de Lorgeril *et al*., 1994). The patient with suspected MI and receiving fish oil or mustard seed oil experienced fewer sudden deaths than the placebo group (Singh *et al*., 1997). The studies have showed inverse relationship between blood levels of long chain n-3 PUFA and risk of SCD (Albert *et al*., 2002). The evidence suggesting an antiarrhythmic effect of n-3 PUFA was provided by GISSI-Prevenzione, controlled trial performed to test the efficacy of an oral administration of n-3 PUFA (1g daily) and vitamin E on morbidity and mortality in 11,323 Italian patients with recent (MI < 3 months; Gruppo Italiano, 1999). GISSI-Prevenzione trial had several strengths. It was adequately sized in a population of patient at high risk of arrhythmia, with a reliable statistical power to show that n-3 PUFA could decrease morbidity and mortality in a clinically and statistically significant manner. As to clinical relevance , it is worth for that every 1000 post-MI patients treated for 1 year with 1 g daily of n-3 PUFA, 5.7 lives were saved. Such protective effect of n-3 PUFA treatment observed in GISSI-Prevenzione is comparable to the results of other drugs which are considered as corner stone in cardiovascular prevention. Indeed, patients enrolled in GISSI-Prevenzione received n-3 PUFA treatment on the top of preventive pharmacological treatments, aspirin, beta-blockers, angiotensin-converting enzyme inhibitors and cholesterol- lowering drugs, as well as lifestyle intervention leading to positive modification of dietary habits with increase of the intake of olive oil, fruit, vegetables, and fish (Barzi *et al*., 2003).

Marine fishes rich in omega-3 fatty acid

Fishes are used to be called as "brain food." Omega-3 are the reason because they are powerful anti-inflammatory that helps to heal all sorts of problems, from poor eyesight to Alzheimer's disease. Fish are the primary source of omega-3 fatty acids, but not all fish are created equal: Here few fishes with high level of omega-3s. (fishcooking.about.com)

Salmon

Salmon is easily the most accessible and familiar of the five top fish for omega-3. The best salmon to get the most omega-3s would be king salmon, also called as Chinook salmon, which are wild-caught from California to Alaska. Interestingly, canned salmon is also high in this good fat. (fishcooking.about.com)

Sardines

Sardines are commonly consumed by humans. Fresh sardines are often grilled, pickled or smoked, or they are preserved in cans. Sardines are rich in vitamins and minerals. A small serving of sardines once a day can provide 13 percent of vitamin B2; roughly one-quarter of niacin; and about 150 percent of the recommended daily value of vitamin B12. All B vitamins help to support proper nervous system function and are used for energy metabolism, or converting food into energy. Also, sardines are high in the major minerals such as phosphorus, calcium, potassium, and some trace minerals including iron and selenium. Sardines are also a natural source of marine omega-3 fatty acids, which reduce the occurrence of cardiovascular disease. Recent studies suggest that regular

consumption of omega-3 fatty acids reduces the likelihood of developing Alzheimer's disease. These fatty acids can also lower blood sugar levels. They are also a good source of vitamin D, calcium, vitamin B12, and protein. Because they are low in the food chain, sardines are very low in contaminants, such as mercury relative to other fish commonly eaten by humans.

Mechanism of Action of Marine N-3 PUFAs

The health effect of n-3 PUFA are mediated by two mechanisms:

A change in the properties of cell membranes

Dietary supplementation with fish oil results in modification of fatty acid profiles, with an increase content of EPA and DHA in plasma lipid, platelets, erythrocytes, leukocytes, cardiac and liver tissue. Very long PUFA decreases the availability of arachidonic acid as a substrate for eicosanoid synthesis and they also inhibit arachidonic acid metabolism. (jn.nutrition.org/content/early/2012/01/24/jn.111.155259)

Regulation of gene transcription

As FAs are incorporated into cell membrane phospholipids, composition of this lipid bilayer is reflected by the composition of FAs ingested. Increasing amount of n-3 PUFA in the cell membrane alters its properties with change of membrane fluidity, permeability, and electrophysiological characteristics (Leaf *et al*., 2003).

Marine N-3 PUFAs and Antiarrhythmic Effects

The reduction of cardiac death with increased intake of n-3 PUFA has been attributed to antiarrhthmic effect. Supplementation with n-3 PUFAs has been found to enrich myocyte membrane with EPA and DHA (Harris *et al*., 2004). This results in change of the cell membrane with effect on ion channels and membrane bound proteins resulting in hyperpolarisation, increasing the depolarizing stimuli necessary to induce an action potential with reduced automaticity. It also affect the transition of voltage-gated sodium channel with more negative membrane voltages, promoting recovery from inactive state and thereby increasing the refractory period. These effects make the myocardium less excitable, especially in ischemic tissue. N-3 PUFAs are capable of inhibiting the voltage-dependent inward calcium current during phase 2 of an action potential. In relation to possible effect on the Na/Ca exchanger and receptors in the sarcoplasmic reticulum this contribute to less intracellular Ca fluctuations and reduced occurrence of after depolarization (Leaf *et al*., 2003). There is also evidence for antiarrhythmic effects mediated through reduced production of proarrhythmic eicosaniods, reduced level of circulating catecholamines (Nodri *et al*., 2009), and a reduced agonist affinity of beta-receptors (Reiffel and McDonald, 2006). The mechanism responsible for improvement in cardiac sympathetic-vagal balance, revealed clinically reduction in the mean heart rate (Mozaffarian *et al*., 2005) as well as an increase in HR variability (Mozaffarian *et al*., 2008). These have been related to the risk of sudden cardiac death (SCD), with increasing HR and decreasing HR variability with adverse outcomes (Jouven *et al*., 2001). Animal experiments have demonstrated beneficial effects of EPA and DHA on the development of ischemia-induced ventricular arrhythmias (Matthan *et al*., 2005), whereas results from human studies are more divergent.

REFERENCES

Albert, C.M., Campos, H., Stampfer, M.J., Ridker, P.M., Manson, J.E., Willett, W.C., and Ma, J. 2002. Blood levels of long-chain n-3 fatty acids and the risk of sudden death. *N. Engl. J. Med. 346, 1113-1118.*

Bang, H. O., Dyerberg, J. 1972. Plasma lipids and lipoproteins in Greenlandic west coast Eskimos. *Acta Med. Scand.* 192, 85-94.

Barzi, F., Woodward, M., Marfisi, R. M., Tavazzi, L., Valagussa, F., and Marchioli, R. 2003. Mediterranean diet and all –causes mortality after myocardial infarction: results from the GISSI- Prevenzione trial. *Eur. J. Clin. Nutr.*57, 604-611.

Billman, G. E., Kang, J. X., and Leaf, A. 1999. Prevention of sudden cardiac death by dietary pure omega-3 fatty acids in dogs. *Circulation* 99, 2452-2457.

Burr, M. L., Fehily, A. M., Gilbert, J. F., Rogers, S., Holliday, R. M., Sweetnam, P. M., Elwood, P. C., and Deadman, N.M. 1989. Effects of change in fat, fish, and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART). *Lancet* 2, 757-761.

Calo, L., Bianconi., L., Colivicchi, F., Lamberti, F., Loricchio, M. L., de Ruvo, E., Meo, A., Pandozi, C., Staibano, M., and Santini, M. 2005. N-3 fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: a randomized, controlled trial. J. Am. Coll. Cardiol. 45, 1723-1728.

de Lorgeril, M., Renaud, S., Mamelle, N., Salen, P., Martin, J. L., Monjaud, I., Guidollet, J., Touboul, P., and Delaye J. 1994. Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease. *Lancet* 343, 1454-1459.

Drevon, C.A. "Marine oil and their effects", Nutrition Reviews, vol.50, pp-29-36, 1992

fishcooking.about.com

Gruppo Italiano per lo Studio della Sopravvivenza nell' Infarto miocardico, 1999. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. *Lancet* 354, 447-455.

Harris, W.S., S.A. Sands, S.L. Windsor *et al*., "Omega-3 fatty acid in cardiac biopsies from heart transplantation patients : correlation with erythrocytes and response to supplementation," *Circulation,* vol.110, no. 12, pp.1645-1649, 2004

He, K., Song, Y., Daviglus, M. L., Liu, K., Van Horn, L., Dyer, A. R., and Greenland, P. 2004. Accumulated evidence on fish consumption and coronary heart disease mortality: a meta-analysis of cohort studies. *Circulation* 109, 2705-2711.

jn.nutrition.org/content/early/2012/01/24/jn.111.155259

Jouven, X., M. Zureik, M. Desnos, C. Guerot, and P. Ducimetiere, "Resting heart rate as a predictive risk factor for sudden death in middle-aged men", *Cardiovascular Research,*vol.50,no.2,pp. 373-378, 2001.

Leaf, A., Y.F. Xiao, J.X. Kang, and G.E. Billman, "Prevention of sudden cardiac death by n-3 polyunsaturated fatty acids", *Pharmacology and therapeutics,* vol. 98, no.3, pp. 355-377, 2003.

Marchioli, R. "Dietary supplementation with N-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial", *The Lancet,* vol. 354, no.9177, pp. 447-455, 1999.

Matthan, N. R., H. Jordan, M. Chung, A. H. Lichtenstein, D.A. Lathrop, and J. Lau, "A systematic review and meta-analysis of the impact of omega-3 fatty acids on selected arrhythmia outcomes in animal models", *Metabolism,* vol.54, no.12, pp. 1557-1565, 2005.

Mozaffarian, D. and J.H.Y Wu, "Omega-3 fatty acids and cardiovascular disease. Effect on risk factors, molecular pathways and clinical events," Journal of the American college of cardiology, vol.58, no.20, pp.2047-2067, 2011.

Mozaffarian, D., A. Geelen, I.A. Brouwer, J.M. Geleijinse, P.L. Zock, and M.B. Katan, "Effect of fish oil on heart rate in humans: a meta-analysis of randomized controlled trials", *Circulation,* vol. 112, no.13, pp.1945-1952, 2005

Mozaffarian, D., P.K. Stein, R.J. Prineas and D.S. Siscovick, "Dietary fish and omega-3 fatty acid consumption and heart rate variability in US adults", *Circulation,* vol.117, no.9, pp.1130-1137, 2008.

Nodri, S., M. Metra, G. Milesi *et al*., "The role of n-3 PUFAs in preventing the arrhythmic risk in patients with idiopathic dilated cardiacmyopathy", *Cardiovascular Drugs and Therapy,*vol.23,no. 1, pp. 5-15,2009

Reiffel, J.A. and McDonald, "Antiarrhythmic effects of omega-3 fatty acids", *American Journal of Cardiology,* vol.98, no.4, pp.0 i50-i60, 2006

Singh, R. B., Niaz,.
M. A., Sharma, J. P., Kumar, R., Rastogi, v., and Moshiri, M., 1997. Randomized, double-blind, placebo-controlled trial of fish oil and mustard oil in patients with suspected myocardial infarction: the Indian experiment of infarct survival -4. *Cardiovas. Drugs Ther.* 11, 485-491.

Task Force of the European Society of Cardiology, and the North American Society of Pacing and Electrophysiology, 1996.

www.fitday.com

www.nhlbi.nih.gov/health/health-topics/topics/cad/

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