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Faculty of Basic Medical Science

Effect of Omega-3 polyunsaturated fatty Acids on atherosclerosis and vascular inflammation

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Abstract:

Atherosclerosis is an inflammatory chronic disease influencing blood vessels and leads to vascular diseases, such as stroke and myocardial infarction. Omega-3 polyunsaturated fatty acids (PUFAs) are included in inflammatory processes. Particularly, omega-3 PUFAs apply anti-inflammatory properties by competing with omega-6 PUFAs and uprooting arachidonic acid in membrane phospholipids, diminishing the generation of pro-inflammatory eicosanoids. Experimental studies and a few clinical trials have illustrated that omega-3 PUFA supplementation may diminish the chance of atherosclerosis and cardiovascular disease. This report portrays the interface between atherosclerosis, inflammation, as well as how omega-3 PUFA supplementation may be valuable to anticipate and treat inflammatory-related disease, atherosclerosis.

Introduction:

Omega-3 are polyunsaturated fatty acids (PUFAs) derived from alpha-linolenic acid (ALA), People are able to metabolize ALA and synthesize distinctive downstream long-chain unsaturated omega-3 PUFAs - including eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA) - through different enzymatic elongation and desaturation reactions, omega-3 (PUFAs) are essential fatty acids and so must be obtained by the diet from dairy items, seeds and seed oils. [(1)]

Atherosclerosis is a chronic inflammatory syndrome that leads to the progressive thickening of large artery walls and reduced blood flow over time, it is characterized by the presence of intimal lesions called atheromas (atheromatous plaques) which are raised lesions composed of soft lipid cores covered by fibrous caps Atherosclerotic plaques can mechanically obstruct vascular lumina which could lead to other complications.[(2,3).]

Inflammation is a protective response involving host cells, blood vessels, and proteins and other mediators that is intended to eliminate the initial cause of cell injury, the initiation of acute inflammation is regulated by several lipid mediators, including the eicosanoids prostaglandins (PGs), thromboxanes (TXs) and leukotrienes (LTs), which have a role in the modulation of blood flood, endothelial permeability, polymorphonuclear neutrophil (PMN) chemotaxis, and platelet aggregation. [(1,4,5)]

The aim of this study is to know in case omega-3 (PUFAs) might act to stabilize atherosclerotic plaques by decreasing the impacts of inflammation.

Materials and Methods:

The first study, An intervention study conducted in patients anticipating carotid endarterectomy showed that omega-3 (PUFAs) which are incorporated from dietary fish oil supplements (giving 1.4 g EPA+DHA/day) into progressed atherosclerotic plaques, to see if supplemention and incorporation of omega-3 is related with structural changes consistent with increased plaque stability.[6]

The second study Named Ocean (Omacor Carotid EnArterectomy iNtervention), utilizing (1.8 g EPA + DHA/day) to discover in case there's an association between a higher EPA content of the plaque and lower plaque inflammation and higher plaque stability. [4]

The third study by Yamano et al. In which 46 patients with coronary atherosclerotic plaque, devided into 2 groups those who received (1,800mg/day of EPA) (n=15) and a control group (n=31), Serial optical coherence tomography (OCT) examinations were performed at baseline and after eight months of follow-up. [7]

Result:

The first study it appeared that due to fish oil supplementation There were plaques with a well-formed fibrous cap, instead of a thin-inflamed cap. Immunohistochemistry was utilized to examine Infiltration by macrophages. It was found that plaques from patients given fish oil were more likely to be less intensely infiltrated with macrophages. [6]

The second study Ocean found that mRNA levels for Certain matrix metalloproteinases (MMPs) proteases which play critical parts in degradation, thinning and weakening of the fibrous cap (MMP-7, MMP-9 and MMP-12) were lower in plaques from patients who had incorporated omega-3 PUFAs, proving that higher EPA content of the plaque lowers plaque inflammation and increases plaque stability.[4]

The third study exhibited a significant increase in the serum EPA levels (50 ± 26 mg/dL to 200 ± 41 mg/dL, $p < 0.001$) in the EPA group, and they did not change in the control group, in contrast the fibrous cap thickness significantly increased in both the EPA group and the control group however, the relative change in the fibrous cap thickness was significantly greater in the EPA group than in the control group.[7]

Discussion:

Experimental evidence suggest that omega-3 (PUFAs) are incorporated quite quickly into advanced plaques and aid in the resolution of inflammation in atherosclerosis and that plaques with a higher EPA content are more stable.

inflammation contributes to the initiation, progression, and complications of atheromas Typically vessels don't bind inflammatory cells. Early in atherogenesis, dysfunctional endothelial cells express adhesion molecules leading to leukocyte adhesion; vascular cell adhesion molecule-1 (VCAM-1), particularly, binds monocytes and T cells. After these cells adhere to the endothelium, they move into the intima by the impact of locally produced chemokines. The crucial step in atherogenesis has been distinguished when monocytes invade and differentiate into macrophages within the intima of the vessels, and whereas internalizing and collecting intracellularly oxidized-LDLs, they continuously change into foam cells. Over time, clusters of foam cells end up as fatty-streaks within the intima of the endothelium. As the disease advances, a few of the endothelial cells adjacent to the atheromatous endothelium start to solidify, forming a hard core called the fibrous cap of the atheroma, which starts to enlarge and occlude the vessel partially to causing progressive narrowing of the arterial lumen.[(1)(4)(5)]

Human inflammatory cells are particularly rich in the omega-6 fatty acid arachidonic acid, but the levels of arachidonic acid and of the omega-3 (PUFAs) EPA and DHA can be altered through oral administration of EPA and DHA. Eicosanoids produced from arachidonic acid play a role in inflammation. EPA also gives arise to eicosanoids which are usually biologically weaker than arachidonic acid-derived eicosanoids. Therefore, omega-3 (PUFAs) play an anti-inflammatory role by promoting the resolution of inflammation.[(1)]

Cyclooxygenase (COX) and lipoxygenase (LOX) enzymes catalyze the conversion of arachidonic acid into a series of pro-inflammatory mediators, including prostaglandins, thromboxanes and leukotrienes. The omega-3 (EPA is also a substrate for arachidonic acid-cascade enzymes (COX and 5-LOX), leading to the production of alternative omega-3 (PUFA)-derived eicosanoids, such as 3-series prostanoids and 5-series leukotrienes, which are inactive metabolites or that appear to lower pro-inflammatory activity compared to arachidonic acid-derived eicosanoids. also , omega-3 (PUFAs) represent the precursors of a series of lipid mediators, including resolvins, protectins and maresins, which are collectively

termed “specialized pro-resolving mediators” (SPMs) which are synthesized through a complex series of enzymatic reactions mediated by (COX-2, P450, and LOX) enzymes. EPA represents the precursor of the E-series resolvins (RvE1, RvE2, and RvE3), whereas DHA leads to the production of three distinct families of SPMs, namely D-series resolvins (RvD1, RvD2, RvD3, RvD4), protectins (protectin D1, known as neuroprotectin D1 [NPD1] when formed in the nervous system), and maresins (MaR1), (SPMs) stimulate key cellular events, such as the diminishing of (PMN) infiltration, macrophage switching to anti-inflammatory phenotype M2, and apoptotic cell clearance.[1][4]

Conclusion:

Although the role of omega-6 PUFAs in triggering systemic inflammation remains controversial, growing evidence highlights the importance of increasing the absolute intake of omega-3 PUFAs in order to reduce CV risk. Indeed, the beneficial CV effects of omega-3 PUFAs may rely on their anti-inflammatory and anti-atherosclerotic properties.

References:

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