Inhibition of vein graft intimal thickening by eicosapentanoic acid: reduced thromboxane production without change in lipoprotein levels or low-density lipoprotein receptor density.

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Marine lipids containing omega-3 fatty acids (chiefly, eicosapentanoic acid [EPA] and docosahexanoic acid [DHA]) may inhibit the development of atherosclerotic vascular disease, but the mechanisms responsible for this putative beneficial effect are unknown. We investigated the effects of EPA and DHA in a canine model of accelerated vein graft arteriosclerosis during a 3-month period. Twenty-five dogs were divided into three dietary groups: group I (control), group II (2.5% cholesterol), and group III (2.5% cholesterol plus 2 gm EPA/day [as MaxEPA]). The effects of EPA on vein graft intimal thickening, platelet and vascular prostaglandin metabolism, lipid and lipoprotein receptor metabolism, and hematologic parameters were assessed. Cholesterol feeding caused a significant 54% increase in graft intimal thickness compared with control animals (124.9 +/- 50.4 vs 81.2 +/- 32.4 micron; p = 0.013), which was prevented by supplementation with EPA in group III (56.9 +/- 30.0 micron; p = 0.001 vs group II). Intimal thickness in group III was not significantly different from that of control. EPA supplementation was also associated with a 38% decline in serum thromboxane levels from 457.0 +/- 129.3 pg/0.1 ml in group II to 283.5 +/- 96.9 pg/0.1 ml in group III (p = 0.007). The alterations in lipoprotein metabolism associated with cholesterol feeding were not affected by EPA: in both groups II and III, serum cholesterol and high-density lipoproteins and liver cholesterol content were elevated and hepatic low-density lipoproteins (LDL) receptor content was reduced. There were no differences between the three groups in terms of vein graft or native vessel prostacyclin production, hematocrit, platelet count, or coagulation parameters. In this canine model, dietary supplementation with marine omega-3 fatty acids reduced the extent and magnitude of accelerated vein graft intimal thickening induced by hypercholesterolemia; moreover, this beneficial effect was associated with lower serum thromboxane production and appeared to be independent of alterations in lipoprotein metabolism or LDL receptor density.

PMID: 3336117 [PubMed - indexed for MEDLINE]