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ARTICLES

Inhibition of accelerated cardiac allograft arteriosclerosis by fish oil

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Accelerated coronary arteriosclerosis remains the most important factor limiting long-term survival of heart transplant recipients, and dietary fish oil supplementation with omega-3 polyunsaturated fatty acids has been suggested to have a protective effect against coronary disease in epidemiologic studies and to inhibit arteriosclerosis in animal experiments. Therefore we tested the hypothesis that fish oil administration inhibits the development of allograft coronary arteriosclerosis by using a heterotopic heart transplant model. Three groups of Lewis rats (n = 10 each) received heterotopic heart transplants from Brown-Norway donors and were treated with cyclosporine intraperitoneally on a tapering schedule. Group 1 received fish oil daily by gavage (2 ml/kg/day; Emulsified Super MaxEpa, Twin Labs, Ronkonkona, N.Y.). Group 2 received an equal amount of safflower oil, as well as aspirin (1 mg/kg/day) and dipyridamole (3 mg/kg/day). Group 3 received safflower oil only. All rats were put to death 110 days later, at which time there was no statistically significant difference in graft function as assessed by palpation (scale 0 to 4, mean = 3.7 +/- 0.5 [+/- standard deviation]; analysis of variance: p = 0.72) or in microscopic grade of rejection (scale, 0 = none to 3 = severe, mean 2.1 +/- 0.6; analysis of variance: p = 0.68) between any of the groups. The coronary arteries were histologically scored for the degree of arteriosclerosis (scale, 0 = normal to 3 = occluded), and a mean grade of coronary disease was calculated for each heart. The fish oil-treated group had significantly less severe allograft coronary arteriosclerosis (analysis of variance: p = 0.005) than did groups 2 and 3 (mean grade 0.23 +/- 0.22 versus 1.04 +/- 0.75 and 0.96 +/- 0.55 (p less than 0.05, Scheffe F test), whereas groups 2 and 3 had similar degrees of coronary disease (p = no significant difference). These data demonstrate that fish oil supplementation inhibited accelerated coronary arteriosclerosis in this cyclosporine-treated heart allograft rat model, whereas antiplatelet agents in these doses were ineffective. Although the mechanism of this protective effect remains incompletely understood, it does not appear to involve enhanced immunosuppression. Fish oil and specific omega-3 polyunsaturated fatty acids should be further investigated as potentially useful agents to ameliorate accelerated allograft coronary arteriosclerosis in other animal species and perhaps eventually in man.

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