COMMENTS AND RESPONSES

Comment on: Satoh-Asahara et al. Highly Purified Eicosapentaenoic Acid Increases Interleukin-10 Levels of Peripheral Blood Monocytes in Obese Patients With Dyslipidemia. Diabetes Care 2012;35:2631–2639

Satoh-Asahara et al. (1) recently reported that treatment with purified eicosapentaenoic acid (EPA; 1.8 g daily) for 3 months increases the serum EPA/arachidonic acid (AA) ratio and interleukin-10 levels of peripheral blood monocytes in association with slight decreases in the pulse wave velocity, an index of arterial stiffness, in obese patients with dyslipidemia. Pulse wave velocity values before treatment with or without EPA were almost within the age-associated normal range (around the age-associated healthy average + 1 SD) in these Japanese subjects. The clinical value of treatment with purified EPA for the primary prevention of atherosclerosis and/or cardiovascular disease, however, remains uncertain.

A recent systemic review and meta-analysis demonstrated that supplementation with n-3 polyunsaturated fatty acids (PUFAs) is not associated with a lower risk of all-cause mortality, cardiac death, sudden death, or myocardial infarction (2). Although in 2000 the Food and Drug Administration recommended 3 g/day of EPA plus docosahexaenoic acid (DHA) to reduce the risk of coronary heart disease, the mean intake of n-3 PUFAs in all studies analyzed was approximately 1.5 g/day (2). The Japan EPA Lipid Intervention Study (JELIS) demonstrated that purified EPA (1.8 g/day) treatment significantly reduces the recurrence of major coronary events in hypercholesterolemic patients with coronary events who are treated with statins (3). Increases in the serum EPA/AA ratio induced by EPA treatment are significantly associated with reduced cardiac death and a reduced incidence of recurrence of myocardial infarction in statin-treated patients with coronary artery disease, as described previously (1). There is no clear evidence, however, that the serum EPA/AA ratio is inversely related to atherosclerosis and/or primary coronary events in subjects without major coronary diseases. Because statins and n-3 PUFAs have similar pleiotropic effects, it may be difficult to demonstrate the effect of supplementation with n-3 PUFAs in patients with a history of statin therapy.

Carotid intima-media thickness (CIMT) is used as a strong marker for atherosclerosis to predict future clinical cardiovascular end points (4). Recent studies reported a differential effect of DHA and EPA on CIMT. Compared with American whites, the Japanese have lower CIMT and more than twofold higher levels of DHA and EPA (5). In addition, DHA but not EPA has an inverse association with CIMT in both Japanese and American whites (5). In the multivariable-adjusted model, DHA but not EPA was a significant predictor of intima-media thickness (5). Thus, DHA may have a more potent antiatherogenic effect than EPA, especially at the levels detected in the Japanese. Treatment with purified EPA has no effects on serum DHA levels (3).

These findings raise questions about whether a decrease in the serum EPA/AA ratio is related to carotid atherosclerosis in subjects without coronary events and whether purified EPA alone reduces major coronary events in hypercholesterolemic patients without a history of coronary events who are not treated with statins.

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