Editorial

Fish Oil and Diabetes
The Net Effect

There is no doubt about it, fish oils are the new dietary craze. Health-food stores and pharmacy shelves are stocked with bottles bearing a label adorned with the smiling face of an atherosclerotic-free Eskimo who devours whale blubber with reckless abandon. Fish oil capsules are definitely in, and Nike training shoes and Sony Walkmans are out. The public has heartily embraced the notion that omega-3 is the effortless way to evade a coronary. We can only assume that a fair proportion of our diabetic patients are also caught up in this new nutritional wave. But should we encourage this behavior?

Omega-3 fatty acids (ω3FAs) are polyunsaturated hydrocarbons believed to be the active components of fish oils.* They modify lipoprotein and eicosanoid metabolism, lower whole-blood viscosity, increase fibrinolytic activity, and decrease arterial blood pressure. In addition, they may alter cell membrane properties and the functions of certain membrane-bound proteins (1). Epidemiologic studies report a significant association between fish oil consumption and decreased incidence of cardiovascular disease (2). Regular ingestion of large amounts significantly lowers plasma triglyceride (TG) concentrations, possibly via inhibition of very-low-density lipoprotein (VLDL) TG and VLDL apolipoprotein B (apoB) synthesis (3–6), increased VLDL removal (7), and augmented secretion of bile acids (8,9).

It is tempting to justify the use of these compounds in diabetic patients for two reasons. First, hypertriglyceridemia has been shown to be independently correlated with coronary artery disease in this population (10–12). Second, in non-insulin-dependent diabetes mellitus (NIDDM), the predominant metabolic disorder of the TG-rich lipoprotein VLDL is overproduction of both VLDL TG and VLDL-apoB (13–16).

However, the close relationship between lipid and glucose metabolism precludes extrapolation of data collected in nondiabetic populations to those with NIDDM. At present, there are only a handful of studies that have evaluated the short-term effects of ω3FAs in diabetic hypertriglyceridemia. Whereas there is general agreement regarding reduction of plasma TG, conflicting reports on glycemic control and low-density lipoprotein cholesterol (LDL-chol) are cause for serious concern.

For example, Popp-Snijders et al. (17) studied six NIDDM subjects (5 of 6 on oral hypoglycemic agents; 2 taking diuretics) who received 3 g/day of ω3FAs for 8 wk. Unlike several subsequent studies, including one by Friday et al. (p. 276) in this issue of *Diabetes Care*, the increase in fasting plasma glucose was insignificant, and insulin sensitivity improved.

Friday et al. followed eight NIDDM males (treated with eucaloric diets) who received 8 g/day of ω3FAs for 8 wk. In this uncontrolled trial, both fasting and meal-stimulated glucose increased, whereas insulin levels and glycosylated hemoglobin concentrations remained unchanged. The adverse effects were most apparent in the more overweight subjects suggesting that ω3FAs

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*Counting from the methyl end of the molecule, the first double bond separates the third and fourth carbon.

may be safer in those who are thinner or concomitantly treated with a hypocaloric diet. Decreases in total cholesterol and VLDL-chol were observed. Whereas mean LDL-chol did not change, it increased in 5 of 8 subjects.

Schectman et al. (18) also reported deterioration of glycemic control in a single-blind 4-wk crossover study of 13 NIDDM subjects taking 1 of 2 doses of ω3FAs versus a fixed dose of safflower oil. Elevations in fasting glucose were seen only at the higher dose (7.5 g/day). Increases in LDL-chol and LDL-apoB were noted, whereas high-density lipoprotein (HDL) was unchanged.

Finally, Glauber et al. (19) suggested that the deterioration of fasting glucose with ω3FA supplementation was associated with elevated basal hepatic glucose output and impaired insulin secretion. In this study, six diet-treated NIDDM males consumed 5.5 g/day ω3FAs for 4 wk. Fasting glucose and meal-stimulated glucose rose by 22%. These elevations were reversed on cessation of ω3FA treatment. No changes were observed in total cholesterol, LDL-chol, or HDL-chol.

The mechanism of glycemic deterioration remains a mystery. Speculations include an alteration in eicosanoid mediators that may play a role in control of insulin secretion in the pancreatic cell (20,21). Effects of ω3FAs on glycemic control in other populations (i.e., those with insulin-dependent diabetes mellitus or among first-degree relatives and others predisposed to develop diabetes) are unknown.

These preliminary studies should draw attention to the possible adverse metabolic consequences of ω3FA therapy in NIDDM. Worsening of glycemic control and elevations of LDL-chol are worrisome and may, in the long run, eradicate any beneficial fish-oil related effects on cardiovascular disease. Diabetic subjects participating in these limited trials have differed in their degree of adiposity, type of antidiabetic therapy, calorie intake, and use of other drugs affecting lipid metabolism. It is obvious that more research is needed to account for the potential role of these confounding variables.

Initial treatment of diabetic hypertriglyceridemia remains optimal glycemic control and a restricted cholesterol, saturated fat diet as recommended by the American Diabetes Association. Weight loss and exercise, independent of qualitative changes in the diet, should be prescribed to appropriate patients. Pharmacologic therapy might be required if these measures fail, usually because of an underlying lipid abnormality. However, our understanding of the role of dietary fats, including omega-6 polyunsaturated, omega-3 polyunsaturated, and monounsaturated, is rapidly evolving. We may expect to see further refinement in dietary recommendations by the 1990s. Until then, we recommend patience and dietary conservatism rather than large amounts of fish oil.

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