Advances in Practice
Therapeutic Benefits of Fish Oils for Patients with Chronic Kidney Disease

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Interest in the therapeutic effects of fish oils began when investigations into the health status of Greenland Eskimos revealed low rates of heart disease, despite high fat intake from fish, seals and whales. Subsequent clinical intervention studies confirmed the ability of fish oils to decrease heart disease by preventing cardiac arrhythmias, inhibiting atherosclerosis, and through their antithrombotic and hypolipidemic properties (1). Additional roles have been identified for fish oils in the management of autoimmune diseases and some types of cancer (2-4).

Recent studies indicate that fish oils might have unique benefits for patients with chronic kidney disease (CKD). Treatment with daily doses of fish oils over a 2-year period slowed the progression of renal disease in patients with Immunoglobulin A (IgA) nephropathy, the most commonly occurring form of primary glomerulonephritis (5,6). Fish may also be a beneficial protein source for patients with CKD undergoing maintenance dialysis therapy. Patients who reported eating fish at least once in a three-day period had a 50% lower mortality rate during a 3-year follow-up period than those who did not report eating fish (7).

The physiological effects of fish oils are attributed to the long-chain, polyunsaturated omega-3 fatty acids they contain. Omega-3 fatty acids are essential fatty acids and important structural components of phospholipid membranes in animal cells (1). The fish and marine mammals consumed by Eskimos contain the omega-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). Green plants are a source of the omega-3 fatty acid alpha-linolenic acid (ALA), from which DHA and EPA may be synthesized.

Today, omega-3 fatty acids are available as fish oil supplements, including Coromega® (European Reference Botanical Laboratories, Carlsbad, CA) and Omacor® (Pronova Biocare, Oslo, Norway) (4,5). In addition, omega-3 enriched spreads and oils are marketed as part of the Smart Balance® product line (GFA Brands Inc., Cresskill, NJ) (8). Renal dietetics professionals may need to provide information on these products as their patients become aware of the potential health benefits of fish oils. This column will review the applications of fish oil therapy to improve health outcomes in patients with CKD.

1. Treatment of IgA nephropathy

IgA nephropathy is an immune complex-mediated glomerulonephritis characterized by deposition of IgA in the kidneys and leading to CKD in 20-40% of those affected (9). While there is no cure for this disease, corticosteroids, angiotensin-converting enzyme (ACE) inhibitors and omega-3 fatty acids have all been investigated as strategies for slowing progression of IgA nephropathy.

Clinical trials with omega-3 fatty acids have shown mixed results overall, but the largest trial provided clear evidence that supplementation with fish oil was accompanied by decreased proteinuria and improved glomerular filtration rate (GFR) in patients with severe IgA nephropathy (10). One hundred and six patients received daily doses of DHA and EPA in the form of four soft gel capsules for 2 years. Follow-up observations averaging 6.5 years indicated that disease progression was significantly delayed.

In an investigation into optimum omega-3 fatty acid dosing to retard IgA nephropathy progression, 73 patients were randomly assigned to receive either high- (2.94g DHA and 3.76g EPA) or low- (1.47g DHA and 1.88g EPA) dose treatments (11). Serum creatinine levels were used to track disease progression. Low- and high-dose omega-3 fatty acid therapies were equally effective in slowing the rate of renal function loss.

2. Lipid-lowering effects

Patients with IgA nephropathy show a significant reduction in serum triglycerides after 6 months of omega-3 fatty acid therapy (12). In addition, serum cholesterol decreases and high density lipoprotein (HDL)-cholesterol increases. Studies of patients undergoing maintenance hemodialysis (HD) also show an association between fish intake and decreased cardiac symptoms. This may occur because omega-3 fatty acids in fish oils decrease serum triglyceride levels as well as ratios of low density lipoprotein (LDL) to HDL-cholesterol, total cholesterol to HDL-cholesterol and triglycerides to HDL-cholesterol (13-15).

In a randomized, placebo-controlled trial, lipid-lowering effects of corn, fish and sesame oils were studied in 60 HD patients assigned to four different study groups (13). Patients in each group received daily doses of corn oil (4.5g), fish oil (1.5g), sesame oil (4.5g) or placebo. Serum triglycerides, total cholesterol, LDL-cholesterol and HDL-cholesterol were measured before and after 2 months of therapy. After supplementary corn and fish oil, HDL-cholesterol increased and LDL-cholesterol decreased significantly. Serum triglycerides also decreased after fish oil therapy. Significant decreases occurred in the ratios of triglyceride to HDL-cholesterol, total cholesterol to HDL-cholesterol and LDL-cholesterol to HDL-cholesterol after fish and corn oil therapy. Sesame oil had no significant effect on lipid profile.

A more recent study showed similar favorable effects of omega-3 fatty acids on lipid profiles in patients with serum creatinine levels between 150-400micromol/L (1.7-4.52mg/dL)[a] (16). The 64 patients in this study were randomly

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[a] To convert micromol/L creatinine to mg/dL, multiply micromol/L by 0.0113. To convert mg/dL creatinine to micromol/L, multiply mg/dl by 88.4. Creatinine of 150 micromol/L = 1.70 mg/dL

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assigned to daily treatment with 2.4g of omega-3 fatty acids or control treatment with olive oil for 8 weeks. Researchers measured fasting lipid and lipoprotein levels in the subjects before and after supplementation. In the group receiving omega-3 fatty acids, there was a significant 8% increase in HDL-cholesterol and 21% decrease in serum triglyceride levels. The hypolipidemic effects of omega-3 fatty acids may therefore help to decrease the incidence of atherosclerosis in patients with CKD.

3. Reduction in hemodialysis graft thrombosis

The synthetic polytetrafluoroethylene (PTFE) graft is the most commonly placed hemodialysis access in the United States (17). However, graft thrombosis is a serious problem and several drugs have been investigated to improve graft patency including heparin, aspirin, calcium channel blockers, ACE inhibitors and warfarin (18,19). Inconsistent clinical results from these drug trials and side effects, including gastrointestinal hemorrhage, have prompted a search for novel strategies to prevent graft thrombosis.

Recently, a double-blind, randomized study was conducted to test the hypothesis that fish oil supplements would decrease the incidence of thrombosis in newly constructed PTFE grafts (17). Twenty-four patients received a daily regimen of either four 1g capsules of fish oil concentrate or four 1g capsules of corn oil. All patients were recruited from the same outpatient dialysis program, and all grafts were placed by the same surgical team. Treatment was initiated within 2 weeks after graft placement and patients were monitored for 1 year or until thrombosis occurred. Only two patients developed graft thrombosis in the group treated with fish oil compared with nine in the control group, and the graft patency rate at the end of the study was 75.6% in patients receiving fish oil supplement versus 14.9% in controls. Thus, findings from this study support the use of fish oils to decrease the incidence of graft thrombosis.

4. Alleviation of pruritis

Up to 86% of patients undergoing maintenance HD therapy experience a poorly localized itching sensation called pruritis (20). Pruritis has been attributed to uremic toxins, calcium-phosphorus imbalance, hyperparathyroidism, changes in vitamin A and magnesium homeostasis, and accumulation of the inflammatory eicosanoid leukotriene B4 in the skin.

Studies in patients with psoriasis have shown significant reduction in skin inflammation and itching following supplementation with fish oil capsules for 8 weeks (21). It is thought that omega-3 fatty acids may exert their beneficial effects by competing for lipoxygenase enzymes, which metabolize arachidonic acid in the skin to inflammatory eicosanoids, including leukotriene B4. Consequently, the effects of essential fatty acids and their metabolites have been investigated in maintenance dialysis patients with pruritis (15,20).

In a double-blind study, 25 HD patients with a history of pruritis were randomly assigned to receive daily supplements of fish oil, olive oil or safflower oil (15). After 8 weeks of treatment, patients who received fish oil had higher levels of DHA and EPA, a greater decrease in arachidonic acid and improvement in symptoms of pruritis.

In a more recent study, 35 maintenance HD patients with pruritis symptoms were randomized to receive six capsules daily of either fish oil or safflower oil for 16 weeks (20). A 3-day food record obtained from each patient before supplementation was analyzed for nutrient content, and patients were instructed to maintain the same eating pattern throughout the study. In addition, symptoms of pruritis were evaluated at baseline and after supplementation by means of a subjective questionnaire. After supplementation, both groups of patients showed nonsignificant reduction in leukotriene B4. However, patients who received fish oil had significantly higher levels of omega-3 fatty acids and a greater, though nonsignificant, decrease in pruritis score compared with patients who received safflower oil.

Summary

Patients with CKD may benefit from fish oil supplementation to delay the progression of renal disease, improve their lipid profile, decrease the incidence of graft thrombosis and relieve pruritis. The ability of fish oils to reduce erythropoietin (EPO) requirements and produce modest increase in serum albumin levels has also been documented (7, 22).

Use of fish oil supplements by patients with CKD appears to carry a low risk of side-effects (22). Taking fish oil supplements with meals reduces the likelihood of gastrointestinal distress. Heparin doses given during HD treatments may also need to be adjusted to prevent prolonged bleeding when patients are using fish oil supplements.

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