Fish Oil Supplementation for Cardioprotection in Chronic Kidney Disease

By Allon Friedman

According to the 2007 National Health Interview survey, fish oil is the most popular dietary supplement used by adult Americans (1). This follows on the heels of decades of well-publicized basic science and clinical research into the biology of long-chain omega-3 fatty acids—the major active ingredient in fish oil—and their influence on a variety of disease processes. Although clinical trials of the use of fish oil in the general population have reported conflicting results, patients with chronic kidney disease (CKD)—in particular end stage renal disease—have several characteristics that may make them an ideal group in which to study and observe benefits from the putative salutary effects of fish oil.

Take, for example, the highly investigated relationship between fish oil and cardiovascular disease. Because of the elevated rates of CKD-associated cardiovascular events and mortality and the questionable efficacy of standard-of-care therapies such as aspirin, β-blockers, and statins in the CKD population, CKD patients offer an excellent study population in which to examine the cardiovascular effects of fish oil. Further strengthening this argument are the types of cardiovascular outcomes observed in CKD patients. Approximately 25 percent of dialysis patients die of sudden cardiac death, a disease entity that may be particularly amenable to the effects of fish oil (2). Finally, CKD patients have among the lowest documented circulating levels of omega-3 fatty acids (3). Inasmuch as circulating levels reflect baseline omega-3 dietary consumption (which is believed to be inversely related to the benefits accrued from omega-3 fatty acid supplementation) (4), CKD patients are an ideal group for fish oil studies. In fact, investigators have already begun to perform such studies.

The first such study was a randomized, placebo-controlled trial performed by Svensson et al. (5) in 206 prevalent Danish patients receiving hemodialysis. The investigators randomized the patients to fish oil (containing 1.7 g omega-3 fatty acids) or placebo and monitored them for 2 years. They reported no improvement in the primary end point, which was a composite of myocardial infarction, angina requiring investigation, transient ischemic attack or stroke, peripheral vascular disease needing interventions, or death. However, they did observe a statistically significant improvement with the use of fish oil in the secondary end points of myocardial infarction (70 percent reduction) and major coronary events (60 percent reduction).

The second study, by Lok et al. (6), tested the effects of fish oil (containing 1.6 g omega-3 fatty acids) on arteriovenous graft patency in a cohort of 201 prevalent Canadian patients receiving hemodialysis. The primary outcome was loss of native graft patency, which fish oil improved by 22 percent (p = 0.06) compared with placebo. The secondary end point of cardiovascular events, a composite of myocardial infarction, congestive heart failure requiring hospitalizations, and cardiac-related death, was significantly improved by fish oil supplementation to a statistically significant extent.

The last study, by Friedman et al. (7), used a case-control design to examine the relationship between omega-3 fatty acid levels and the risk of sudden cardiac death in a cohort of 400 patients in the United States who were beginning long-term hemodialysis. They found an inverse and steeply graded relationship between serum omega-3 fatty acid levels at baseline and the odds of dying of sudden cardiac death during the first year of dialysis, even after controlling for a variety of major risk factors.

In general, these studies support the need for a well-powered randomized controlled trial to determine definitively whether fish oil improves cardiovascular outcomes in hemodialysis patients. That being said, in which patients should such a study be performed? The ideal population would be one in which dietary omega-3 fatty acid intake and blood levels are low, because this is the population most likely to benefit. Interestingly, patients in the Danish trial had levels that were higher than those in the Canadian and especially United States study populations, perhaps explaining in part why its findings were negative. On the basis of this criterion, it seems that North American hemodialysis patients, whose dietary omega-3 fatty acid consumption is among the lowest according to the medical literature, offer an excellent population in which to study the cardioprotective effects of fish oil. In light of the large potential benefits and low risks of fish oil supplementation, such a trial should be enthusiastically welcomed by the nephrology community.

Allon Friedman, MD, FASN, is affiliated with the Indiana University School of Medicine in Indianapolis, IN.

References