Preventive Use of N-3 Fatty Acids

To the Editor:

In the editorial “N-3 fatty acids: priority for post–myocardial infarction clinical trials,” Dr Scott Grundy1 (somewhat cautiously) endorsed the need for a trial to test the hypothesis that ω-3 fatty acid (FA) supplements will reduce risk for coronary death in patients randomized in the immediate post–myocardial infarction period. We support this recommendation, but we differ with Dr Grundy’s assessment of the strength of the evidence for recommending increased intake of eicosapentaenoic and docosahexaenoic acids (EPA and DHA) today. The GISSI Prevenzione study, although not placebo-controlled (blinding capsules is not easy), did, however, provide compelling evidence from a randomized trial of 11 000 postinfarction patients that 850 mg of these two FA will reduce total mortality by 28% (P<0.03) and risk for sudden death by 47% (P = 0.01).2 This appears to be due to a unique ability of ω-3 FA to reduce fatal ventricular arrhythmias that are independent of, and additive to, the cardioprotective effects of standard cardiovascular pharmacotherapy (eg, aspirin, angiotensin-converting enzyme inhibitors, statins, and β-blockers). These findings are supported by a large and consistent body of evidence correlating fish intake with reduced risk of fatal coronary events.3–5 We disagree with the implication that physicians should refrain from utilizing these FA until further clinical trials are completed (which would delay implementation for many years). Additional large, randomized, placebo-controlled trials using ω-3 fats to affect clinical end points are needed, but there are multiple population studies supporting the cardioprotective effects of ω-3 FA, and the randomized trials that have been reported with 0.5 to 3 g of EPA+DHA have been uniformly positive. The dearth of large, randomized, placebo-controlled trials is largely due to the pharmaceutical industry’s lack of interest in promoting an agent that cannot be patented. To require the same level of proof as a new drug for a nutritional product designated as “generally recognized as safe” by the Food and Drug Administration with strongly suggestive benefits is in our view excessively conservative. Taking an evidence-based approach, the American Heart Association has endorsed the use of about 1 g of EPA+DHA for patients with coronary disease.5 At worst, following this advice is harmless; at best, thousands of lives will be saved.

William S. Harris, PhD

James H. O’Keefe, Jr, MD

Mid America Heart Institute

Saint Luke’s Health System

Kansas City, Mo


Response

In response to my editorial “N-3 fatty acid: priority for post–myocardial infarction clinical trials,” Drs Harris and O’Keefe indicated that I cautiously endorsed the need for a clinical trial to test whether N-3 fatty acids will reduce risk for coronary death in patients in the immediate post–myocardial infarction period. In fact, I was strongly enthusiastic about such a trial, but one that will focus on prevention of fatal arrhythmias. The available literature appears to support the need for such a trial. However, until such a sudden-death trial is carried out, I am less enthusiastic about a trial to test the benefit of N-3 fatty acids on acute coronary syndromes. The literature seems less compelling in this area.

Drs Harris and O’Keefe further disagreed with my interpretation of the literature regarding the strength of the evidence of completed trials, notably the GISSI Prevenzione study,1 which suggested that treatment of post–myocardial infarction patients with N-3 fatty acids will reduce sudden death. They support the recent American Heart Association position statement2 that favored routine use of N-3 in such patients. There is always some controversy as to when there is enough clinical trial evidence to recommend routine use of therapy.

With regards to N-3 fatty acids, my view accords with that of the National Cholesterol Education Program’s Adult Treatment Panel III (ATP III) report,3 which places their use in the category of “optional,” based on physician discretion rather than recommended routinely. The ATP III position is somewhat at odds with the AHA position, the latter providing a stronger recommendation. In my view, the best way to resolve this difference in reading of the evidence is by more clinical trials. Such is the standard approach of evidence-based medicine. In the meantime, I favor the ATP III position of optional therapy, whereas I recognize that others espouse recommended therapy.

Drs Harris and O’Keefe end by saying that “at worst, following this advice [routine use] is harmless; at best, thousands of lives will be saved.” All of us have heard this argument before for other therapies. Many investigators would argue that routine use of a “harmless” but ineffective therapy is not as harmless as it might at first seem. Finally, there is the issue of quality of product. At present, there are no preparations of N-3 fatty acids that assure purity of product or consistent fatty acid composition that can be used routinely in clinical practice.

Scott M. Grundy, MD, PhD

University of Texas Southwestern Medical Center at Dallas

Center for Human Nutrition

Dallas, Texas


Preventive Use of N-3 Fatty Acids
William S. Harris and James H. O'Keefe, Jr

Circulation. 2003;108:e139
doi: 10.1161/01.CIR.0000099902.61378.96
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circ.ahajournals.org/content/108/19/e139

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial
Office. Once the online version of the published article for which permission is being requested is located,
click Request Permissions in the middle column of the Web page under Services. Further information about
this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/