

## Fish Oil, Secondary CVD Prevention Link Still Murky

BY MITCHEL L. ZOLER  
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NEW ORLEANS — The value of fish oil for the secondary prevention of cardiovascular-disease events was placed in some doubt with results from a diet study that involved about 200 patients.

"We saw no difference between the American Heart Association's Step II diet and the Mediterranean diet for preventing major cardiovascular events in patients following a myocardial infarction," Dr. Katherine R. Tuttle said at the annual meeting of the American College of Cardiology.

In addition, patients who followed either of these diets had significantly fewer cardiovascular events during follow-up than did patients who had usual care and did not adhere to a formal diet, said Dr. Tuttle, director of research at the Providence Medical Research Center in Spokane, Wash.

"What was compelling was how well both diets did compared with a usual-care diet. Clearly, patients who are motivated to adhere to a diet will do substantially better" than will those who aren't, commented Dr. Paul Ridker, director of the Center for Cardiovascular Disease Prevention at Brigham and Women's Hospital in Boston.

But some experts were skeptical about whether the new results, which involved a modest number of patients, proved that a diet rich in omega-3 fatty acids from plant and fish sources was no better than the standard level of omega-3 fatty acids in the AHA Step II diet. This aspect of the study involved 50 patients who began and 45 who completed the Step II diet, and 51 patients who began and 48 who completed the Mediterranean diet.

The study had "too few patients" to make any firm conclusion about the incremental value of a diet rich in omega-3 fatty acids, said Dr. Christie M. Ballantyne, director of the Center for Cardiovascular Disease Prevention at Baylor College of Medicine, Houston.

In the 2006 revision of its diet and lifestyle recommendations the AHA stated: "Patients with documented coronary heart disease are advised to consume about 1 g of EPA [eicosapentaenoic acid] and DHA [docosahexaenoic acid] per day, preferably from oily fish, although EPA and DHA supplements could

be considered in consultation with their physicians." This AHA recommendation has been in place for several years. EPA and DHA are the major omega-3 fatty acids found in fish oil.

The Heart Institute of Spokane-Diet Intervention and Evaluation Trial (THIS-DIET) randomized 101 patients within 6 weeks of a first myocardial infarction who were willing to go on one of the study diets. Another 101 similar patients who were not willing to be assigned to a diet were followed in a usual-care control group. All three groups were similar at baseline for clinical and demographic measures. Patients in the diet group had seven individualized diet counseling sessions spaced throughout the first 2 years of the study, as well as at least six group sessions a month. Patients were responsible for preparing their own foods.

The major difference between the Mediterranean and Step II diets was in the level of omega-3 fatty acids consumed. For a focus on this difference, management of patients in all three groups was structured so that patients would not lose weight during the study, an effect that would have confounded the results. The strategy worked: Patients in the study did not have significant weight loss.

The study's primary end point was the composite rate of death, nonfatal myocardial infarction, and nonfatal stroke. After a median follow-up of 46 months, the rate was identical in both diet groups, with a total of eight events in each group. In contrast, there were 40 events in the 101 patients in the control group (compared with a total of 16 among the 101 patients who began the two diet groups). The calculated odds ratio was a 67% risk reduction for patients in either diet group compared with control patients, a statistically significant difference, Dr. Tuttle said.

"We were surprised that there was no difference" between the two diets, she said in an interview. If the finding is confirmed, it would be good news for many American patients with coronary disease who don't like fish, she added. "These were mostly older, white patients in the U.S. Northwest, and a lot of them had trouble increasing their intake of fish and olive oil. They did, but they didn't like it." Subsequent studies also need to test the hypothesis that it's the intensive intervention that's most important, and that any diet would be effective in this context, Dr. Tuttle said. ■

## Diesel Exhaust Fumes Promote Myocardial Ischemia in CHD

BY BRUCE JANCIN  
Denver Bureau

NEW ORLEANS — Brief inhalation of dilute diesel exhaust at levels comparable with those encountered curbside along city streets promotes myocardial ischemia in patients with coronary heart disease, said Dr. David E. Newby at the annual meeting of the American College of Cardiology.

He presented the first-ever study in which patients with known CHD were exposed to air pollution in an effort to pinpoint the mechanisms underlying the epidemiologic association between air pollution and increased cardiovascular morbidity and mortality.

"Not everybody believes air pollution is linked to cardiovascular disease, particularly pressure groups backed by the automobile industry," said Dr. Newby, professor of cardiology at the University of Edinburgh.

He and his coinvestigators in Edinburgh and at Umeå (Sweden) Univer-

sity briefly exposed 20 patients with prior MI to either dilute diesel exhaust at a concentration of 300 mcg/m<sup>3</sup> or to filtered air during intervals of moderate exercise or rest in a double-blind



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DR. NEWBY

crossover study conducted in a special chamber. All of the patients had stable CHD, having previously undergone coronary revascularization. All were on standard evidence-based medications for secondary prevention.

Exposure to diesel exhaust caused a threefold increase in the magnitude of exercise-induced ST-segment depression: a mean 49 mcV of ST depression, compared with 17 mcV of ST depression while breathing filtered air during exercise. In addition, blood levels of tissue plasminogen activator—a potent endogenous clot dissolver—declined significantly after patients were exposed to diesel exhaust, providing a second specific mechanism to explain the link between air pollution and cardiovascular events.

In a previous study of healthy volunteers, Dr. Newby and his colleagues showed that brief exposure to real-world levels of diesel exhaust caused impairment of arterial vasodilation. The World Health Organization has estimated that nearly 1 million deaths per year are attributable to inhalation of polluted air.

The British Heart Foundation funded his study. ■



Nearly 1 million people a year die from inhaling polluted air, says the World Health Organization.

## Weight Gain in Migraineurs May Raise Cardiovascular Risks

BY MICHELE G. SULLIVAN  
Mid-Atlantic Bureau

CHICAGO — Patients who gain at least 5% of body weight while taking prophylactic migraine medications experienced changes in clinical markers that could indicate increased risk of cardiovascular disease, said Dr. Marcelo Bigal at the annual meeting of the American Headache Society.

"Given that migraine and being overweight or obese are independent risk factors for cardiovascular disease, and obesity is a risk fac-

tor for migraine transformation and greater pain during migraine attacks, weight gain—including that associated with medical treatment—may have particularly important health implications in migraine patients," said Dr. Bigal, of the Albert Einstein College of Medicine, New York.

He and his colleagues compared weight change with clinical markers of cardiovascular disease risk and headache treatment response in migraineurs participating in a large trial of topiramate and amitriptyline for migraine prophylaxis. The 331 patients were

randomized to either topiramate 100 mg/day or amitriptyline 100 mg/day for 26 weeks. Most of the patients (67%) stayed at a steady weight. Weight gain occurred in 16% and weight loss in 17%. Most of those who lost weight (91%) were taking topiramate, and most of those who gained weight (87%) were taking amitriptyline.

There were no significant differences in medication response by weight change category. Patients with weight gain and loss had similar reductions in the mean frequency of monthly migraine episodes (−2.7 vs. −3.0).

However, weight change did influence the clinical markers of cardiovascular disease risk. Those who gained weight experienced significant elevations in mean diastolic blood pressure, glucose levels, heart rate, total cholesterol, and LDL cholesterol, compared with those who lost weight.

Patients who gained weight also had increases in their levels of C-reactive protein (CRP), gaining a mean of 1.8 mg/L. Patients who lost weight had a decline in CRP of 1.9 mg/L. Although the difference was not statistically significant, Dr. Bigal noted, it may be

clinically meaningful. "CRP values of less than 1 mg/L predict low cardiovascular risk, values of 1-3 mg/L predict average risk, and values greater than 3 mg/L predict high risk [according to Centers for Disease Control and Prevention and the American Heart Association]. Given that migraine is itself a risk factor for cardiovascular disease, weight gain in migraine patients may have particularly important health implications."

The study was sponsored by Ortho-McNeil Janssen Scientific Affairs L.L.C. Dr. Bigal is a consultant for the company. ■